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OTOLARYNGOLOGY

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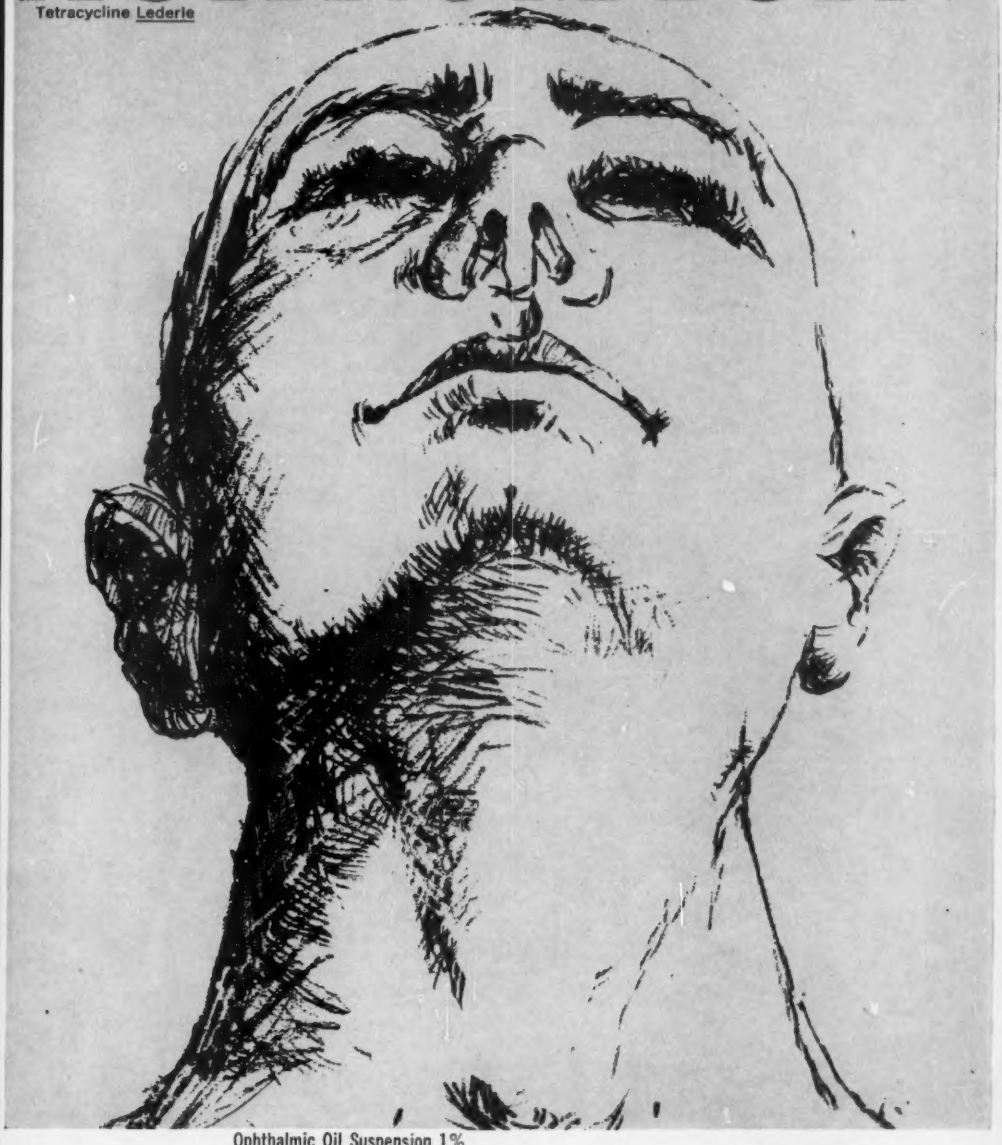

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A Second Golden Decade in Rhinology

Advances of the Past Ten Years

H. C. GUNDERSON, M.D., Toledo, Ohio

"Outstanding and significant contributions to nasal septum surgery, corrective nasal surgery, anatomy and physiology were made during the first decade of the 20th century. . . . It is conceivable that our successors sometime hence will again enjoy surveying the records of rhinology during the first decade of our century and I trust that it would not be too daring to hope that they may discover that a second 'golden' decade flourished about 50 years later." So wrote Cottle in March of this year.[1] No doubt these observations have stimulated many to consider the advances of the past 10 years, for there has indeed been a quickening of interest once again in rhinology, and the past decade is indeed worthy of being considered a possible second "golden" decade. There is ample evidence that the rhinologist and his colleagues in allied fields have taken a new look at rhinology, reappraising established ideas and techniques and developing new concepts and procedures. It may be that we are on the threshold of such rich activity as heart surgery has been going through.

Stimulating articles have appeared in the readily available otolaryngological literature pertaining to basic phenomena, not always of immediately apparent clinical importance. There is growing awareness among rhinologists of the importance of new knowledge in embryology, anatomy, histology, endocrinology, and physiology. The ground substance of the respiratory tract, for instance, has been discussed by Rawlins,[2] who gives it a position of considerable importance, and does not treat it merely as an inert tissue whose single duty it is to hold the anatomical structures together. He cites its action as a barrier against infection, its role in the action of enzymes and hormones, and in allergic and nonallergic inflammations. Weisskopf and Burn,[3] likewise, point out that the ground substance of the nasal turbinates is not merely a packing and protective material but an important physiologically active substance which takes a primary place in the activities of the nose. The venous networks of the nasal mucosa were studied by Batson,[4] who has some beautiful photographs in his article. He shows that the mucosa is pervaded throughout by interlacing venous networks without valves and communicating everywhere with each other and with the veins of the underlying bone, the thickness of this venous network paralleling the thickness of the mucous membrane itself. Ballenger[5] and Tremble[6] bring our knowledge up to date concerning respiratory cilia. Dixon et al.[7] observed in the by-passed nose of laryngec-

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Director of Otolaryngology, Mercy and Children's Hospitals and Toledo Clinic.

Presented at the 4th Annual Meeting of the American Rhinological Society, Chicago, Oct. 14, 1958.

tomized patients that areas of squamous metaplasia gradually were replaced by ciliated columnar epithelium and became always moist, that the color changed from pink to pale purple, that the surface temperature was found to be higher and more uniform than normal, and that the patients were subject to infrequent colds.

Robison [8,9] has reported some interesting ideas and concepts about the lymphatic drainage of the nasal chambers and paranasal sinuses and its relationship to allergic sinus disease. He describes a lymph-pump mechanism of the nasal apparatus and the sinuses and the retropharyngeal lymph nodes into which this mechanism drains. It would seem that his ideas are worth following up.

From time to time, observations of the effect of the autonomic innervation of the nasal mucosa are made.[10] The swelling of the nasal mucosa and increase in secretion associated with interruption of the sympathetic fibers suggests a new approach to the problem of atrophic rhinitis, whereas the interruption of the parasympathetic nerve supply causing just the opposite, with shrunken and dry mucous membranes, suggests the need for investigating the use of this knowledge in the treatment of vasomotor rhinitis.

As might be expected, considerable attention has been directed during the past decade to air currents in the nasal chambers and moisture exchange. Proetz's article of 1951 is worth rereading, of course.[11] Becker and King [12] have reviewed the literature and say it is "evident that there is no real unanimity of opinion with regard to what pathway air generally takes as it passes through the nose." They describe their well-thought-out experiments in dogs and conclude that studies carried out on canine cadaver heads and on the living dog yield inspiratory air-flow patterns that are in no way similar. From their evidence, one must be obliged to consider the possibility that our conceptions of air flow through the living nose are not well grounded. Becker and King did find distinctly different routes of air flow during inspiration and expiration in the living dog. They found that air was not drawn over the olfactory mucosa in ordinary breathing but was by sniffing.

Scott,[13] Negus,[14,15] and Cramer [16] take a second look at the concept that the main function of the nose is air conditioning. It might well be that the turbinates were developed primarily as a temperature regulating apparatus, and only secondarily are they useful as structures ancillary to the lungs in preparing the air to proper temperature and degree of humidification for reception by the alveoli.

It is becoming increasingly evident that patho-physiologic processes and so-called syndromes of disease are not necessarily attributable to one etiologic agent and that the same biologic pattern may be called forth in response to a variety of noxious experiences. It has been shown that life situations productive of anxiety, hostility, guilt, and feelings of frustration and resentment can be accompanied by nasal hyperfunction, hyperemia, swelling of the nasal mucosa, hypersecretion, and obstruction to nasal respiration. The reaction accompanying these changes can be suppurative in character, with an increase in the neutrophil and eosinophil content in the nasal secretion. These observations have been made by Wolf,[17,18] who points out that pain commonly accompanies the nasal hyperfunction. He adds that when such a pattern is unduly sustained, pathologic changes occur, which give rise to or prolong troublesome symptoms and can become important in the pathogenesis of true chronic nasal disease.

Considerable attention has been given to the fundamental anatomical structures and their practical relationships. The Straatsmas,[19] for instance, report on the anatomical relationship of the lateral nasal cartilage to the nasal bone and to the cartilaginous nasal septum in 20 cadavers. Converse [20] gives an excellent detailed review of the anatomy of the cartilaginous structures of the nose. A nasal aponeurosis has been de-

scribed surrounding and enveloping the cartilaginous structures as well as the tip of the nose.[21] Klaff[22] has studied the anatomy of the nasal septum and especially of the premaxilla. He has gathered information from many sources, including his own dissections. He reviews the literature, reports on his own anatomical observations, and describes the surgical anatomy and technique; this certainly is an article to study well.

Articles devoted to the tip of the nose, the nasal vestibule, the columella, and the upper lip help improve our understanding of these important structures.[23] In particular, Cottle's article[25] on the structure and function of the nasal vestibule is worth reading more than once. He suggests that disharmony between the structures of the external nasal pyramid and the internal nose is a cause of nasal illness. The characteristic anatomy of the Caucasian nostril is compared with that of the Negro and of intermediate races; changes in the vestibule throughout life are discussed, and birth injuries are dwelt upon, it being noted that more than 5% of children born after prolonged or difficult labor have a nose dislocated from the midline. It is pointed out that the measurement of the child's head from the occiput to the tip of the nose is practically always the longest or greatest diameter.

Williams[26] reports on studies made by himself and others of the anthropological nasal index and the cephalometric index, from which the clinical nasal index has been developed. He maintains that the clinical nasal index is intimately associated with the size and shape of the nose. This index is greater in the colored races, Indians and Orientals, than in the white races. He compares the two basic anatomic types of noses, the Caucasian and the Negro, and suggests that each has a characteristic functional pattern. The concept of the clinical nasal index should provoke considerable discussion and stimulate renewed interest in the study of basic anthropological measurements and the influence of climate.

Several authors have made interesting contributions to our understanding of the effect of the thyroid gland on rhinologic problems. From his observation of 130 cases, Proetz reports[27] that thyroid deficiency can result in two types of nasal conditions: a red, dry, irritated, and chapped or a pale, wet, and boggy mucosa, with increased tendency to nasal infection and allergy, correctible or at least influenced by administration of thyroid extract alone. Headache and nasal obstruction were reported as prominent symptoms and a B.M.R. was reported helpful, but not infallible, in diagnosis or evaluating treatment. Hollander[28] reported on 202 patients, of whom 126 yielded minus B.M.R. readings. He states that, between the clinically obvious hypothyroid state and the normal, there is a "no man's land" in which the results of therapeutic tests can serve as convincing evidence of functional irregularity and points out that poor results in many throat and nose disorders can probably be accounted for by lack of appreciation of the endocrine system.

Increasing attention is being devoted to stress and disease and the corticosteroids. Selye's[29] article requires complete reading with full attention for proper digestion. Dolowitz and Dougherty[30] give an interesting account of the influence of the steroids in inflammation in otolaryngology, and Flynn[31] discusses their use and abuse, stating that routine use in ordinary infection is certainly to be avoided. Rawlins[32,33] also discusses the subject ably and emphasizes the importance of the ground substance in so-called collagen diseases. Cottle has reported on the use of hyaluronidase in rhinology.[34]

Hansel has discussed the problem of vascular headaches and related phenomena in medical otolaryngology.[35,36] He notes that in the otolaryngological practice of today, 80% or more of the problems encountered require medical treatment because of such problems as allergy, respiratory and other infections, headaches, poor nutrition, endocrinopathies, and psychosomatic

states. In his opinion, allergy, infection, and headaches are the most important problems. As usual, his articles make good sense and are well worth rereading. Boies [37] has made some very practical suggestions as to causes and therapy of head pain, and Hilsinger [38] discusses allergic headaches in an article which bears rereading by all interested in this important subject.

It must be noted that excellent progress is being made in the field of treatment of cancer of the nose and associated structures. Sooy [39] gives an excellent report on septal tumors and includes 11 illustrative case reports. Lederer et al.[40] also report on tumors of the nasal cavity and emphasize the external approach, while Bordley [41] reports on lateral rhinotomy and transection of the septum anteriorally for exposure of intranasal tumors. Schuknecht [42] and Tabb [43] report on their experiences with carcinoma of the paranasal sinuses and emphasize the importance of early radical surgery followed by irradiation.

Several notable articles dealing with nasal fractures have appeared in the past 10 years. Becker [44] reviews his experiences with 100 cases and lists seven signs in their order of frequency; epistaxis, swelling of the nasal dorsum, ecchymosis of the eyes, tenderness of the dorsum, x-ray evidence of fracture, obvious nasal deformity, and crepitus of the nasal bones. In most cases, two or three signs and symptoms were present, but in 40% of the cases, the fracture was not definitely visible by x-ray. He found greenstick fractures only in children in his series, and they were most difficult to diagnose. He states that early reduction is the procedure of choice within the first few hours, if possible, but observes that fractures seen as late as two or three weeks after injury can be satisfactorily reduced; he stresses the value of proper internal and external splinting. Becker, as well as Aagesen, Morrison, and Sputh,[45] advises examination under general anesthesia in children in any doubtful case. Fomon et al.[46] point out that many difficult reconstructions, tedious submucous resections, and extensive scar excisions could be avoided if proper treatment were instituted at the time of the original surgery.

Recently, attention has been directed again to the role of the rhinologist in pituitary surgery. Hirsch,[47] a pioneer in this field, gives an interesting review of the history and reports on his extensive experiences. Heck et al.[48] provide a very comprehensive review and report on a considerable experience with this type of surgery. They discuss the normal anatomy, pathology, hormonal effects, diagnostic points, and techniques of anesthesia and surgical intervention. They conclude that the transeptal-sphenoid pituitary operation is an excellent procedure with very low postoperative morbidity and mortality. They feel that in some ways the rhinologic approach is superior to craniotomy.

Congenital choanal atresia is a problem to which rhinologists and others have given considerable attention, and an article by Owens [49] is an excellent exposition of the transpalatine approach. This article is well written and illustrated and bears study by those interested in this problem.

Epistaxis is a problem which will always be with us. Several noteworthy reviews have been presented in the past decade and bear study. The authors point out the inadequacy of our present knowledge of the clotting mechanism and pathological predisposing conditions as well as the room for improvement in both medical and surgical treatment.[50-53] The techniques of electrocoagulation of bleeding points, nasal packing, ligation of the carotid and ethmoidal arteries, and submucous resection in the control of nasal hemorrhage are all discussed.

Another matter in which the otolaryngologist finds himself compelled to take an interest is that of malignant exophthalmos. Boyden [54] and Walsh and Ogura [55] describe rhinologic techniques that give immediate and satisfactory recession of the eye through surgical decompression by way of the sinuses.

From time to time, articles appear in our literature bringing out the importance of nutritional inadequacy in the production of symptoms in our field of work. Rosenvold,[56] in an instructive article, reports on 500 patients from his private practice. He points out that nutritive failure in varying degrees is prevalent in half or more of the American population, and most deficiencies are multiple and involve more than one nutrient element. Since many of these persons develop otorhinolaryngological symptoms, it behooves us to learn how nutritional requirements are being met in our patients. Rosenvold points out that nutritional guidance can be made simple yet effective in clinical practice.

There are many patients in our practices who fail to respond to almost everything we can do for them, and we are obliged to consider attack on the turbinates themselves for what is usually considered to be some form of vasomotor rhinitis. House[57] reports on 102 patients he has treated by submucous resection of the anterior one-third of the inferior turbinal bone and observed for a period of two years thereafter. The description of his technique is well worth studying. Shahinian[58] has written comprehensively about submucous diathermic coagulation in patients with vasomotor rhinitis. The description of his technique and of his methods of calibrating his diathermy instrument is well worth study.

It seems to me that in the field of surgery of the deviated nasal septum with obstruction and with associated external deformity the greatest advances have been made in rhinology in the last 10 years. Most of us present in this room were taught, during our residencies, a circumspect method of submucosal resection of bone and cartilage without any effort at reconstruction of skeletal integrity, and with great respect being paid to the cartilage comprising the free anteroinferior border of the septal cartilage and also the cartilage beneath the dorsum. In those days of not so very long ago, the external nose was given no serious consideration by the average rhinologist. However, in the past decade, a veritable flood of articles dealing with the anatomy, the physiology, and the surgery of the nasal septum and external nasal pyramid has appeared in our literature. Most of the credit for this development must go to Samuel Fomon,[59-62] who brought to rhinologists a knowledge of rhinoplastic procedures and teaching methods which made it possible for many rhinologists to acquire at least a basic understanding of rhinoplastic techniques and their application in nasal surgery. Others, notably Cottle and Goldman,[64-70] have carried on with teaching courses as well as contributions to the literature. So many articles have appeared by those mentioned and others that only an exhaustive review could possibly be fair to the efforts of all the men who have given time and study to the problems involved. As a result of these teaching courses and the dissemination of knowledge by the printed word, septal surgery now has advanced to the stage where minimal injury is produced; skeletal integrity is reconstituted; increasingly satisfactory methods of handling the anteroinferior part of the septal cartilage and the cartilage beneath the dorsum are available to us, and our ability to correct associated abnormalities in the nasal pyramid, premaxilla, and nasal spine is much increased. Surgery in children is now feasible. Many interesting, illuminating, and provocative ideas about nasal physiology have been advanced by some of these authors, and much has been done, but there is no doubt that much remains to be done, especially as regards corroborative evidence that can be convincing to those still skeptical. Cottle, Goldman, Fomon, and their associates, Williams, Huffman, Lierle, Becker, Converse, Riggs, and Wexler, have all advocated that the septal framework should be preserved with or without manipulation of the rest of the nose; that it is proper to correct not only the septal injury or deformity, but also other abnormalities which affect normal functioning of the nose, and that correction

of the anatomic variations and restoration of the normal physiology should be the objective of the rhinologist.[73,74]

As knowledge of rhinoplastic techniques has become available to the rhinologist, he has expanded his scope of activity and become increasingly aware of the importance of surgery of the tip of the nose and the nostrils as well as the deformities of the columella caused by septal cartilage deformity. Considerable attention has been given to the base of the nose and the cartilage comprising the tip as well as the columella, and the literature contains so much meat that rereading the original articles is imperative.[75-79]

Nasal implants and grafts have been given considerable attention in the past decade.[80-83] Cottle and his associates, Riggs, Fomon, and Pressman have written informative articles on this subject.[84-87] Barry [88] has done an interesting study on reactions to implants in dogs.

Implants are of value, of course, in the treatment of ozena, as has been known a long time. Proud [89] stimulated renewed interest with his acrylic implants. Ogura [90] and also Saunders [91] have reported on cases of atrophic rhinitis in which bone grafts were used. Ersner and Alexander [92] report on 12 cases of atrophic rhinitis and ozena, treated by a modified one-stage rhinoplastic procedure. Cottle has made many interesting observations on these matters and, in a very well and clearly written article recently published,[93] advances his view that atrophic rhinitis is the final stage of a series of pathologic changes that may have started long before they became recognizable as clinical entities. He suggests that they started in a small way owing to inadequate blood supply, with developing atrophy in one or more areas of the nasal mucous membrane, and this early condition he refers to as "early nasal atrophy." He emphasizes the importance of recognizing the condition and early diagnosis. He suggests a regimen of medical and surgical measures including the newer antibiotics, corticosteroids, endocrines, and vasodilators. He discusses bone-grafting procedures to the septum and floor and lateral walls of the nose, nose-narrowing, and nose-reducing operations. His experiences warrant the advice that the surgical procedures be carried out in suitable cases at intervals of 10 to 20 months for 5 to 10 years, thus making possible rehabilitation even with extreme involvement. He gives an admirable description of the surgical techniques employed.

The material so far reviewed in this report compels one to conclude that, in the past decade, rhinologists have experienced a rejuvenation of interest in their work and have had many advances brought to their attention by leaders in the field.[94-96] Many articles that were abstracted in preparation for this paper have not been mentioned because of limited time and space for the purposes of this meeting. For those who wish to delve into the subjects further, it will be rewarding to peruse the bound volumes of the various otolaryngological journals available in almost any well-stocked medical library. However, the more serious student will be obliged to refer to journals in allied fields as well as the *Acta oto-laryngologica* and supplements, which in this decade have been a gold mine of information from the experimental point of view. It is to be hoped that some day bound volumes of the transactions of the American Rhinologic Society will be available also.

In summary, then, it can be said that a review of the readily available literature for the past decade suggests that it has been indeed a second "golden" decade in rhinology. Inspiring advances in knowledge have been made, and the rhinologist has had a rejuvenation of spirit and interest. By careful additional work, especially in the laboratory, he must validate or reassess, if necessary, his new concepts of nasal physiology and their surgical implications.

Allow me to close in a personal vein. I am sure that I echo the sentiment of all the members of our Society in saying that for us the past decade has been a rich and

"golden" one. It seems especially appropriate here to acknowledge the great debt we owe Dr. Cottle, the founder of our Society. With his inspiration and leadership we have been privileged to share, each in his own measure, in some of the progress of the past 10 years. He, especially, has given us the opportunity to work together, to improve ourselves, and to share with others. With leaders like him to guide us, we should see even greater advances in rhinology in the next 10 years.

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External Hyperostosis of the Mandible Angle Associated with Masseteric Hypertrophy

A New Entity

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It is our purpose to describe the bony clinical and radiologic findings in cases of masseteric hypertrophy and to report a new entity associated with it—external hyperostosis of the angle of the mandible. The clinical material upon which this study is based consists of 28 cases which were subjected to a multidisciplinary study at Winter Veterans Hospital and other psychiatric institutions in Topeka, Kan., by Guggenheim and Cohen and associates.[1] The observations of these workers accord with the opinion of Gurney,[7] shared by Kern,[13] that the masseteric enlargement is a work hypertrophy caused by the habit of jaw clenching. It has been found that the presence of this condition indicates a severe underlying emotional disturbance. A central problem of the patients concerned has to do with disposal of excess quantities of oral-aggressive energy.

As pointed out by Boldt,[4] Barton,[14] and others, patients with this condition frequently present themselves to dentists or tumor surgeons because of the suspicion of a dental complication or of neoplasia of the

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The radiologic observations recorded herein were carefully studied and approved by Drs. Patrick Peartree, William Jurgensen, and Raymond McDonald, of the Department of Radiology, Creighton University School of Medicine.

From the Departments of Otolaryngology and Radiology, Creighton University School of Medicine. Formerly of the staff of Winter Veterans Hospital, Topeka, Kan. Dr. Cohen is now staff psychologist at Veterans Hospital, Philadelphia.

Fig. 1.—Young Negro man with bilateral chronic, suppurative parotitis.

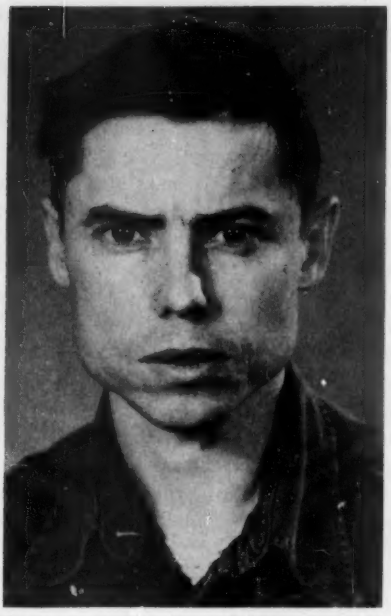


Fig. 2.—A young adult with bilateral masseteric hypertrophy.

parotid gland (Figs. 1 and 2).* Barton [14] claims to have seen more than 30 cases referred to various tumor boards over a 10-year period. Inevitably, these cases will be referred for radiologic study of the jaw.

The radiologic findings reported in the literature [2-14] may be very briefly summarized. Legg [2] and Adams [8] state that "prominence of the angles" of the mandible can sometimes be detected by careful palpation. Coffey,[5] Tempest,[10] and Kern [13] mention absence of bony abnormality in x-rays of their cases. Maxwell and Waggoner [9] observed that wide-flaring mandible angles can be unassociated with any masseteric hypertrophy, while marked muscle enlargement may exist with mandibles of normal shape. Barton [14] attributes flaring of the angles to the pull of the overactive hypertrophic muscle.

Our own material yielded completely negative x-ray findings in only five cases, and none of these exhibited the more extreme degrees of masseteric hypertrophy. Eight cases showed protruding-mandible angles. The majority, 14,† showed an additional feature nowhere mentioned in the extant literature [2-14]—external hyperostosis of the involved mandible angles. X-ray studies were also made on 14 hospitalized "controls," ‡ 5 of whom were found to exhibit lateral flaring of the mandible angles; the remainder had perfectly normal contours. No hyperostoses were seen in this group.

If hyperostoses be excluded from these statistics and attention focused upon the instances of true lateral flaring of the mandible angles (the two conditions being roentgenologically distinguishable), it is seen that one out of 3.5 instances of masseteric hypertrophy exhibits flaring, as compared with one out of 2.8 for the control group. These figures lend little support to Barton's [14] contention that the pull of the hypertrophied masseter influences the configuration of the mandible in this respect. It has been shown [1] that masseteric hypertrophy originates most often in late adolescence or early adulthood, by which ages the definitive shape of the mandible has certainly been determined.

External Hyperostosis of the Mandible Angle (Hyperostosis externa anguli mandibulae, l'hyperostose du gonion)

These growths are readily distinguished § from laterally flared mandible angles by two

* In actual practice the differential diagnosis between masseteric hypertrophy and other conditions is not difficult, but biopsy is justified in doubtful cases and cosmetic correction sometimes indicated.

† In one case no film was taken. Several cases have been studied more recently (Council Bluffs, Iowa) but are not included in this study.

‡ Controls in this study were selected on the basis of sex, age, psychiatric and major somatic (if any) condition, length of illness, educational level, intelligence quotient, and, of course, absence of masseteric hypertrophy.

§ Data from direct observation of mandibles are not available at this time. In a future report concerning anthropological aspects of masseteric hypertrophy, it is hoped that some comparative

(Footnote continued on next page)

Fig. 3.—Mandible of normal contour, showing no eversion or hyperostosis.

features: irregularity of contour and irregular density (Figs. 3-7). The border of the growth may present an irregularly scalloped appearance or protrude as a more or less sharp, irregular spike—features which suggest that the deviation from normal has occurred after the basic contour of the mandible has been determined and that it consists of new bone laid down by an irritated periosteum. The irregularity of density sometimes assumes the appearance of multiple cystic rarefactions, such as are seen in degenerative osteoarthritis (Figs. 6 and 7).

One can only speculate as to why these hyperostoses appear in certain cases while others with equal masseter hypertrophy fail to develop them. The explanation may lie in the well-known individual differences in the responsiveness of connective tissues (periosteum) to trauma.

Hyperostoses of the mandible (and maxilla) have been extensively described in the past. Hrdlička [15] cites 43 authors,[16-20] himself included, in a monumental study (1940). The principal subject of this lavish attention is the lingual hyperplasia of the lower jaw, common in Eskimos and other arctic peoples but exhibited by every human group extensively studied (Fig. 8). This lesion has been variously referred to as "hyperostosis of the lower jaw" (Danielli, 1884), "mandibular hyperostosis" (Hrdlička, 1910), "mandibular torus" (Fürst and Hansen, 1915), and *"torus alveolaris mandibulae"* (Schreiner, 1935). Hrdlička objects to the generally used term "mandibular torus" on the ground that the

radiographic data from Sioux specimens in The Smithsonian Institution will be available. The present study is confined to radiographic appearances in the living. An experienced plastic surgeon of our acquaintance (Albert Black, M.D., Omaha) has operated upon four cases and encountered no hyperostosis, at least, none of a size requiring bone resection.

Fig. 4.—A case of mild bilateral masseter hypertrophy associated with eversion of the mandible angles but showing no hyperostosis.

Fig. 5.—A case of mild eversion of the mandible angles, showing no masseter hypertrophy whatever.

Fig. 6.—A case of marked bilateral masseter hypertrophy, showing marked hyperostoses, larger on the left side, but no eversion of the mandible angles. Note "cystic" rarefactions.

Fig. 7.—A case of marked bilateral masseter hypertrophy with hyperostosis of the left mandible angle but no eversion. Note "cystic rarefactions." There is also an insignificant hyperostosis (not well shown) on the right side. The soft tissue shadow of the enlarged masseter, apparent on the original film, is not reproduced here. This patient also had achalasia of the esophagus.

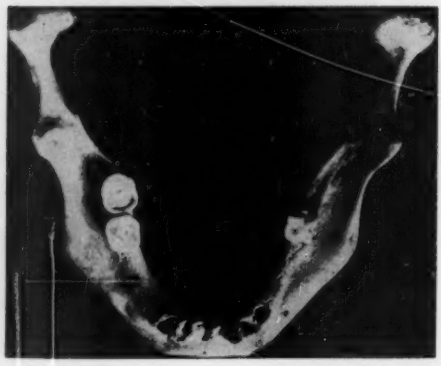
Fig. 8.—Lower jaws showing extreme forms of (lingual) hyperostoses. From below upward: Kodiak Island female, No. 374633, U. S. N. M.; Kodiak Island male, No. 374675; Kodiak Island female, No. 374611, U. S. N. M. Reproduced with permission from Hrdlička, A.: *Am. J. Phys. Anthropol.* 27:1-67 (June 29) 1940; Philadelphia, Wistar Institute of Anatomy and Biology.

growths described occur in the form of "irregular welts, or multiple tuberosities, or single knobby bulges, or in a combination of some or all of these forms" (compare *hyperostosis externa anguli mandibulae*), whereas the Latin *"torus"* indicates a "rounded swelling or bulge." He notes that lingual hyperostosis may be "perceptibly larger or heavier on one side than the other," but so far, he states, there is no predominant lateralization. Guggenheim and Cohen [1] found essentially the same to be true of masseteric hypertrophy (with or without associated hyperostosis), except that this condition can be exclusively unilateral.

Buccal and lingual *maxillary* hyperostoses are also described, the former being commoner. Of particular importance for our purposes is Hrdlička's description of *"external* mandibular torus" (Fig. 9), a lesion clearly not identical with the external mandibular hyperostosis described by us. Hrdlička's [15] description of it is quoted in full:

> Before relinquishing the subject it may be of some interest to call attention to a case shown in the lower figure, plate II. This is a normal jaw of a pre-Colombian middle-aged Indian woman from Chicama, Peru (265, 352, USNM). As seen from the picture there is a pronounced bilateral dull enlargement of the bone externally, on the oblique line, opposite M_1. I have seen two or three similar, though less pronounced, cases of this anomaly in our Peruvian material. *The enlargement shows no roughness or irregularity* [italic ours]. I do not know how to explain it. *External buccal hyperostoses comparable to the lingual ones, have never been reported,* nor have I seen the condition in any other except the Peruvian series. Whatever the condition may be, the term "external mandibular torus" seems in this case both justified and fitting.

Fig. 9.—Mandible of pre-Columbian Indian woman, showing external mandibular torus. Reproduced with permission from Hrdlička, A.: *Am. J. Phys. Anthropol.* 27:1-67 (June 29) 1940; Philadelphia, Wistar Institute of Anatomy and Biology.



We believe that the lesion described by us may be said, as Hrdlićka writes of lingual mandibular hyperostosis, to be "neither exostoses, which are either incidental, senile, or pathological formations; nor osteomae, which are individual isolated bone tumors; nor neoplasms of any pathological nature. They are plainly mere hyperplasias or hyperostoses of normal bone." This pathological diagnosis is concurred in by Kajava (1912), Hooten (1918), Schreiner (1935), and others.

Regarding pathogenesis, Hrdlićka quotes Duckworth and Pain [16] (1900) as stating, "These thickenings are due to a subperiosteal deposit, the exciting cause of which is uncertain." Hrdlićka [17] (1910) was of the opinion that the growth was of "functional origin, the result of extraordinary pressure along the line of teeth most concerned in chewing; yet its occurrence in infant skulls indicates that at least to some extent the feature is already hereditary in these Eskimos." In 1930, Hrdlićka [18] stated, "The lingual mandibular hyperostoses are physiologic formations, developed in answer to the needs of the alveolar portions of the lower jaw. They could be termed *synergistic hyperostoses.*"

Weidenreich [19] (1936), in his report on the Sinanthropus mandibles, described lingual hyperostoses in two specimens and felt that the growths were correlated with actual robustness of the jaws and not their need of strengthening. He felt that he was dealing with a primitive hominid characteristic (true also of torus palatinus). Drennan [20] (1937) stated, "These tori may manifest themselves as a response to some functional stimulus, but. . . . they can only appear in individuals with the appropriate genetic background."

Finally, Hrdlićka [15] (1940) dismisses all but functional factors, stating:

> What is well known to every anatomist and anthropologist is, that wherever there is a material or prolonged heightening of muscular action, the bones to which the muscles concerned are attached respond by thickening of the bone and frequently its enlargement. There are good examples of this in the deltoid tuberosity of the humerus, etc. . . .

In a carefully reasoned argument, he concludes that the etiologic factor must be "the quantity and quality of food with their direct effects upon the structures of mastication." He excludes "some abnormal factor, some weakening of the organism and with it that of the jaws, predisposing to bone proliferation" on the basis of lack of evidence, stating, "All human lower jaws possess the possibility of their development. . . ." Clearly, however, some individual predisposition (compare the cited "individual differential responsiveness to trauma of connective tissues") is necessary, since all persons subsisting upon the "pathogenic" diet do not develop the condition.‖

In keeping with Weidenreich's [19] concept of the atavistic nature of lingual hyperostosis, we must admit that unknown constitutional factors, perhaps of an atavistic nature, may also play a role in the formation of the bony lesion described by us. Indeed, it is not clear why any particular person, endowed with what we have found to be the necessary but not sufficient constellation of psychic characteristics, develops masseteric hypertrophy at all. We are dealing here with one among many possible ego defenses, the choice of which, in appropriate circumstances, is dictated by factors largely unknown—very possibly of a constitutional nature.

642 Forest Dr.

Addendum

After the present paper was submitted for publication, Dr. Albert Black, of Omaha, brought to our attention a report by F. Masters, N. Georgiade, and K. Pickrell,¶ in which external bony growths at the

‖ Hrdlićka's reasoning is a good example of the fallacy of attributing a complex phenomenon (actually a series of events) to a single so-called "cause."

¶ The Surgical Treatment of Benigh Masseteric Hypertrophy, *Plast. & Reconstruct. Surg.* 15:215-221 (March) 1955.

mandible angles are described. We wish to acknowledge the priority of these authors.

They state as follows:

An unusual anatomic variation of the angle of the mandible may have some etiologic significance. In the case presented by Adams,# and in all six cases in this series, a definite, rough, spine-like projection of cortical bone along the anterior surface and free margin of the angle of the mandible, formed an integral part of the insertion of the hypertrophied muscle. This osteoma-like projection increases markedly the available area of muscular insertion, and the lateral projection of the angle of the mandible changes the direction of contraction of the anterior fasciculas of the masseter which inserts on its surface. *The significance of this bony spur is not clear, but its presence has been a uniformly constant companion of the masseter* [italics ours].

Their x-ray photo illustrating this phenomenon fails to show the hyperostosis—a difficult feat as we know from our own experience.

The authors state that in every instance the removed bony spur proved to be cortical bone and that a definite diagnosis of osteoma could not be made.*

The authors modestly credit Adams with the first description of an external mandibular hyperostosis, but a review of Adams' article reveals that he spoke only of correction of "the over-prominence of the mandible at the angle." He did not distinguish between flaring and hyperostosis and did not describe the pathologic condition of the involved tone.

No. 8 in our references.

* Hrdlička,[15] on the pathology of lingual hyperostosis, quoted on p. 679.

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Syndromes of the Head and Neck of Dental Origin

I. Pain Caused by Mandibular Dysfunction

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History

The diseases and disturbances which are attributed to disorders of the temporomandibular articulation present one of the most controversial problems in medical and dental science. Freese[1] states that as early as 3000 B.C. the anatomy of this joint and "dislocation of the mandible" were known. He very aptly brings the history of the subject up to date, and so no further remarks will be necessary at this time.

The Problem

The subject of temporomandibular joint disturbance and resultant pain or other sequelae was brought to the attention of the medical and dental professions by Costen, in 1934.[2] Dentists had noted these phenomena even before Costen described the *syndrome* to which his name has been given.

Costen[3-5] described his symptom-complex as occurring uniformly in disturbed temporomandibular joint function. The symptoms were described as follows: (1) *ear symptoms,* such as loss of hearing, stuffy sensation in the ears, buzzing tinnitus, earache, and dizziness without nystagmus; (2) *pain* in the form of headache about the vertex or occiput or behind the ears and a burning sensation in the throat, tongue, and side of the nose; (3) *miscellaneous symptoms,* such as dryness of the mouth and herpes of the external ear canal and buccal mucosa, and (4) *trismus.*

It was Costen's belief that all these symptoms were caused by altered temporomandibular joint function, due to overclosure of the jaws resulting from loss of posterior teeth. He maintained that pain arose as a result of pressure on or near the chorda tympani and the auriculotemporal nerves. Other authors[6-8] also reported improvement of symptoms following the restoration of a normal relationship of the condylar heads within the glenoid fossae by the technique of raising the bite. Although widely practiced at first and still in vogue today, Costen's form of treatment, as well as the existence of the syndrome itself, has been questioned.[9-11]

Unquestionably, no single factor can be responsible for all these varied symptoms. It is the *interaction* of the nervous, muscular, and vascular systems, at least in the affected region, which requires our attention. Further investigation should enable us to define more accurately the detailed symptomatology and its relationship to the various nervous and vascular networks.

Pain and dysfunction in the form of reduced mandibular movements were the symptoms found most frequently in several hundred cases by one investigator,[12] while the symptom-complex described by Costen was not found. The symptoms in these cases were precipitated by the sudden or continuous stretching of the masticatory musculature: yawning, excessive biting, prolonged sessions of dental treatment, or proprioceptive changes caused by sudden or extensive alterations in the dental occlusion through treatment. Female patients out-

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numbered the males with a ratio of 4:1. Treatment was primarily *spasmolytic*, consisting of ethyl chloride spray on the affected musculature and of intramuscular infiltration with a local anesthetic, followed by exercises of the masticatory muscles.

A recent study [13] conducted for 11 years on 899 selected cases of temporomandibular arthroses with pain showed that 551 patients benefited from dental care. In this study, the ratio of females to males was 3.5:1. A distinctive, though variable, pain pattern emerged from this study, as 20 different groupings of pain distribution were noted. This type of pain was concentrated at the origins and insertions of muscles, and the joint was found to be the commonest site. Treatment was primarily *prosthetic*, with employment of a temporary acrylic splint to discover the optimal occlusal level, followed by permanent occlusal reconstruction after close observation over a suitable period of time.

In both studies, the pain described by the patients was a constant, *dull ache*, as differentiated from the sudden, sharp, and intermittent pain of the neuralgias. Pains were also reported remote from the temporomandibular joints, namely, in the jaws, neck, and shoulders.

The Need for Further Studies

There appears to be a widespread belief that the problems of Costen's syndrome, or of temporomandibular dysfunction in general, are subject to controversy. Many otologists feel disinclined to deal with such problems. Yet, dentists frequently report good therapeutic results which cannot be brushed aside.

Partly to satisfy our own curiosity, and partly with the hope of helping to clarify this problematic matter, we decided to investigate it once again. We also had a good practical reason for a systematic study: Many patients are seen in our clinics whose complaint of earache or other cranial pain cannot be satisfactorily solved with routine otolaryngologic management. These patients, it was felt, may represent cases of mandibular dysfunction.

In view of the complex variety of the symptoms commonly associated with Costen's syndrome, we decided to approach the problem from three distinct viewpoints, namely, the complaints of (1) *pain*, (2) *ear noises*, and (3) *hearing loss*. Otherwise, the evaluation of symptoms, treatments, and results may become too involved to be convincing. For practical reasons, we decided to begin with a study of pain associated with certain abnormalities of the masticatory mechanism. The problems of tinnitus, hearing loss, and other associated symptoms will be the subject of subsequent investigations.

Differentiation of Cranial Pain

When dealing with the emotionally tinged problem of pain, it is good to recall certain basic facts of neurophysiology. At first, we have to be sure of what we are talking about. Although all pain sensations are ultimately transmitted by nervous pathways, they may originate in various structures. Pain affecting the regions of head and neck can be caused by pathologic processes involving the nerves, the muscles, or the connective tissues. Among these, muscle pain appears to be of special importance for our subject. Therefore, we have to give some thought to the physiology of the masticatory musculature.

Whenever a patient suffering with pain around the face consults his family physician, he tries to determine the etiologic factors. If the cause is found, it is treated accordingly and the symptoms subside. However, there are many cases which do not respond, and it is in these that the *dentofacial factors* are often overlooked.

Generally speaking, the factors causing pain about the head or predisposing to it are many. Nutritional or deficiency disease can impair the metabolism of the tissue cells, making them more susceptible to injury of a type that could give rise to pain. Other deficiencies, such as in carbohydrates

and oxygen, also predispose to metabolic disturbance. Once a focus of local pathology has become established, it usually irritates the surrounding nerves, causing pain.

Some of the common causes of *nerve pain* are direct trauma; indirect trauma on the perineural tissues causing pressure; traction pressure on the vascular supply, leading to anoxia and ischemia; extension of inflammation from neighboring tissues; invasion of a nerve by specific organisms or by a neoplasm.

When *muscles* are traumatized, compressed, overexercised, or in a state of sustained contraction or hypertonicity, they react with characteristic pain which is often accompanied by *spasm*. Muscles may be subject to pain as a result of deficiencies, such as in carbohydrates, or from the accumulation of products of metabolism as a result of muscle function.

Connective tissues, such as deep fasciae, tendons, ligaments, and periosteum, may be the location of pain resulting from excessive traction or from injury from neighboring inflammatory processes. With regard to bone, the periosteum is very sensitive to traction tension. Cancellous bone is less sensitive to noxious stimuli and compact bone hardly at all.

It is the task of careful examination to differentiate between these different types of pain. As a general rule, *neuralgic pain* is recognized by demonstrating tenderness at the points of exit of sensory nerves, such as at the trigeminal foramina. *Myalgic pain* is characterized by localized tenderness of the affected muscles and by their spastic contraction, such as in myalgia of the sternocleidomastoideus, which hurts while being pinched. *Periosteal pain* shows sensitive trigger areas which may also appear thickened to the palpating finger.

General Considerations of Muscle Physiology

The body contains various types of muscle fibers, which fall into three distinct groups, namely: skeletal, intestinal (smooth), and cardiac. The muscles associated with motor functions in the head and neck region are composed entirely of skeletal muscle fibers.

When dealing with muscle pathology, one must bear in mind certain physiologic characteristics of skeletal muscle, such as chemical action within the muscle fiber, its nutrition, and the phenomena of fatigue and tetanus. One of the most important facts is that skeletal muscle functions properly only when the normal distance is maintained between the origin and insertion of the fibers. Striated *muscle loses tone* and strength when the distance between these two points is shortened. On the other hand, *muscle tone is increased* beyond normal when the distance between origin and insertion is increased.[6]

Muscle has inherent properties: those residing in the muscle itself and others controlled by impulses reaching it from the nervous system. Both play an important role in considering the resolution of the problems of dental pathology. Any given muscle may, on different occasions, act (1) as a prime mover, (2) as an antagonist aid in coordination, or (3) as an antagonist to neutralize an unwanted movement produced by another prime mover.

Muscles can contract either isotonically or isometrically. When they contract *isotonically*, they shorten but retain equal tension; if they contract *isometrically*, they increase tension but do not shorten and thereby retain their length. By contracting isotonically, muscles act as movers. By isometric contractions they act as holders, stabilizers, or positioners. In addition, muscles contract in preparing for their subsequent relaxation in order to brake or balance the moving contraction of their antagonists.[14]

Anatomical Remarks Concerning the Muscles of Mastication

The muscles of the face are arranged around each orifice in a perfect functional manner. This includes a sphincter and an

opposing dilator arrangement which are specific for each orifice. In the eyelids and the lips these antagonistic systems are well developed, while around the nostrils and particularly around the ear lobes they are vestigial in man.

There is general agreement regarding the elevating action on the mandible by the temporal, masseter, and medial pterygoid muscles; about the retrusive action of the posterior fibers of the temporalis, and about the anteroposterior and lateral movements of the mandible by the simultaneous contraction of the medial and lateral pterygoid muscles on one side.

Confusion can result from analyzing muscles outside their true functional groups, whereby the primary action of a muscle can be overlooked and some undesired secondary effect misinterpreted as the primary action. Further confusion arises from the fact that during forced movements muscles not normally in contraction may be brought in as accessory muscles. Any basic study should refer to normal tranquil movements if we are to understand abnormalities upon further examination. A review of the literature has revealed that no complete agreement has yet been reached on the following problem.

The suprahyoid and infrahyoid muscles require accurate and more comprehensive analysis if we are to understand their actions. Last [19] drew attention to the fact that muscles anatomically in contact do not necessarily share a common action, "In the functional sense, there is no such group as the 'suprahyoid muscles,' and Thompson and Brodie,[15,16] McCollum,[17] Moyers,[18] and others fall into error in assigning a common action to muscles whose only common property is, in fact, that they lie together above the hyoid bone." Last further states that the suprahyoid group is not a group at all but consists of muscles with very different actions. The digastric muscle helps to depress the mandible; the mylohyoid elevates the floor of the mouth, and the geniohyoid and stylohyoid determine the length of the floor of the mouth. They are all either opposed or assisted synergically by the infrahyoid muscles whose actions are of little importance to our present discussion.

Muscles are arranged in the body according to the best engineering principles, thus providing for conservation of energy. Furthermore, advantage is taken of effective leverage and assistance available from gravity. The following muscular functions influence the dental mechanism: posture maintenance, deglutition, mastication, and facial expression.

With regard to the problem of *posture maintenance,* we may consider the shoulder girdle, clavicula, sternum, and scapula as the fixed base of operations. The head may be said to virtually teeter on the atlanto-occipital joint. Since the center of gravity of the head lies in front of the occipital condyles, it naturally follows that definite force must be applied to hold the head erect, a force which is provided by the large muscles of the back of the neck. Several groups of muscles are attached directly or indirectly to the anterior part of the head, whose functions tend to add to the force of gravity, and thus to the load on the posterior cervical muscles, requiring thereby greater bulk and strength on their part. The most important of these anterior cranial muscles are the masticatory and the supra- and infrahyoid groups. They constitute a sort of chain: With the mandible and hyoid bone, to which they are attached, they join the cranium to the shoulder girdle. It follows that within this chain the movements of the mandible and hyoid bone can occur independently of each other and of this functional chain itself.[16]

Last [19] agrees that the head is supported by the posterior cervical muscles, but he differs with Brodie on those muscles that are the opponents of the extensors. Brodie describes them as a chain that extends from the skull to the pectoral girdle and consists of the muscles of mastication that elevate the mandible, the suprahyoid muscles, and

the infrahyoid muscles. Last believes that Brodie has completely ignored the prevertebral flexor muscles (rectus capitis, anterior and lateralis, and longus capitis) and the sternomastoid, which are the true flexor muscles of the skull on the spine.

Brodie quotes Sherrington's Law of reciprocal inhibition of muscles but he misapplies it in his assessment. The tonus of his anterior chain of muscles is that of its weakest link. If the suprahyoid muscles invoke a contraction of the temporal and masseter as they do during the elevation of the floor of the mouth in swallowing, they likewise invoke a relaxation of the infrahyoid muscles. Thus, the head would be jerked back into extension each time we swallow if the infrahyoid muscles were indeed a factor in normal head posture.

Last [19] continues his discussion by stating that contraction of the temporal and masseter muscles certainly accompanies the mylohyoid stage of swallowing, but for a very different reason from that assumed by Brodie. The mylohyoid is organized in two halves which together form a gutter-shaped sling beneath the tongue. Contraction of the muscle elevates the tongue, making the floor of the mouth more shallow. This elevates the tongue, and if the teeth are held in occlusion, produces an increased pressure in the tongue, forcing it back into the oropharynx. This is the normal mechanism of the first stage of swallowing. Increased pressure on the tongue can be produced by mylohyoid contraction only if the mandible is held in occlusion by its elevators. Otherwise, the midline raphe of the mylohyoid would be fixed below the tongue and the contracting fibers of the mylohyoid would pull the mandible down.

Etiology of Craniofacial Pain

As every practitioner knows, the etiology of pain in the area of the head and neck comprises a great variety of causative factors. Instead of an endless enumeration, suffice it to say that the possible causes may be divided into three main groups: (1) *general systemic disease*, such as cardiovascular, renal, or arthritic; (2) *local pathology*, such as in the ears, nose, sinuses, throat, or cervical spine, and (3) *abnormalities of the masticatory mechanism*, the topic of our present discussion.

Dentists are used to the following classification of oral conditions which may give rise to pain: dental malocclusion with or without malposture of the jaw; loss of teeth and the failure to replace them; loss of vertical height between the jaws; poorly fitting dental prosthesis; faulty habits, such as pipe-clenching or unilateral mastication, and disease of the temporomandibular joints. A frequent further cause of facial pain is the muscle imbalance due to malposition of the mandible, occlusal prematurities, and muscle spasm.

Several investigators have attributed the pain associated with temporomandibular joint disturbances mainly to the masticatory muscles.[20-22] In such conditions, the pain and limited activity are associated with "trigger areas." These are small areas in the myofascial structures which are hypersensitive to stretch and give rise to muscle spasm with referred pain. It has been stated [23] that excessive opening of the mouth, as occurs in a yawn or during prolonged dental visits; sudden pain in the teeth, or severe pain in the area of the mouth can evoke a compensating extended contraction similar to the action of a stretch reflex of other skeletal muscle. This would result in a prolonged tonic spasm of the jaw muscles, such as is found in bruxism. Since there is no relaxation, the resulting dysfunction of the temporomandibular joint produces more pain, leading to a vicious cycle.

We must always bear in mind that malposition of the jaws does not necessarily result in pain or other disturbances. Whether or not such conditions occur depends not only on the presence of abnormal stresses or strains but also on the adaptive capacity of the person. This quality varies from one person to another, and it also varies with age, health, emotional status, etc. This accounts for malocclusions of considerable extent in some persons not causing any

symptoms, while the slightest deviations in others result in extreme discomfort.

Wolff [24] has stated that when the pain-sensitive structures about the head are stimulated, the muscles of the head contract. If this stimulus be short-lived, muscle effects are also brief. If, on the other hand, the painful stimulus from deep structures persists, long lasting contractions of the muscles of the head and neck and even of the jaws and face take place. Such sustained contractions result in pain and tenderness of the muscles involved.

Symptomatology of Pain Caused by Mandibular Dysfunction

In evaluating the causes of facial pain, we have to analyze the subjective complaints and the objective findings. The following *subjective complaints* are of importance: There may be varying degrees of discomfort, from a dull sensation to extreme pain. The duration of this pain may be intermittent or quite constant. The pain may not be restricted to the site of the trouble but may travel other pathways.

Other *associated symptoms* may include subjective ear noises; headaches of the migraine variety, affecting chiefly the occipital or vertex region; clicking in the temporomandibular joint while chewing; dizziness; difficulty with swallowing; tingling or burning sensation of the side of the tongue, and various other complaints which may not immediately appear to be related to the occlusal difficulty, such as impaired nasal respiration.

Upon examination, one may detect any of the following *objective findings:* crepitus in the temporomandibular joints; stiffness, asymmetrical movements, or hypermotility of these joints; locking of the jaws with ankylostoma; muscular spasms, or impaired speech when the front teeth fail to occlude for the correct articulation of the sibilant sounds.

Method of Investigation

At the Ear, Nose and Throat Department of the New York Eye and Ear Infirmary, the residents have been taught to recognize the principal types of mandibular pathology, such as dental malocclusions, deviations of the depressed mandible from the midline, and displacement of the heads of the condyles in their fossae.

All patients visiting the clinic are first carefully examined for possible ear, nose, or throat disease of local or systemic origin. Those patients presenting any of the symptoms discussed above and not suffering from any other illness are then referred for dental consultation.

Audiograms are taken whenever the patient complains of earache, ear noises, or hearing loss. The frequency and intensity of tinnitus are measured in the customary manner. These permanent records permit objective comparisons of any therapeutic results.

Dental examination takes place right in the ENT clinic for the benefit of constant consultation between all interested specialists. This examination includes the search for tender muscle regions or "trigger areas." Simple treatments, such as ethyl chloride spray or procaine infiltrations, are given at the same time, if necessary.

Diagnosis of Dental and Mandibular Pathology

Dentistry now has reached that stage of development where it is ready to aid the otolaryngologist and other medical specialists in the differential diagnosis of head and neck syndromes. In addition, it offers scientifically sound corrective procedures for restoring the proper position of the jaws in the three dimensions of space.

It is obvious that a precise and complete diagnosis is essential before any therapeutic measures are undertaken. The dentist requires the definite exclusion of all local pathology not pertaining to his field. Again, a large variety of possible causes have to be considered by his referring advisors.

(1) *Aural, nasal, and nasopharyngeal disease.* It is necessary to rule out the existence of more probable nasopharyngeal conditions, such as lymphoid hypertrophy, cysts, or

tumors. Audiometric tests should be taken to determine the precise type of hearing loss that may exist.[10,25] The dentist must also be advised what portion of a detected perceptive loss may be due to physiologic presbyacusis.

(2) *Adenopathy,* especially of the parotid gland.

(3) *Disorders of neural origin,* such as isolated or associated paralyses of cranial nerves.

(4) *Collagenous disease,* like rheumatoid or osteoarthritis, and scleroderma which may affect the temporomandibular joint.

(5) *Bone dyscrasias,* including osteoporosis.

(6) *Traumatic disorders,* such as fractures and sprains of the mandible or its joints.

(7) *Neoplasms* involving the temporomandibular joints; and

(8) *Psychogenic factors.*

After this exclusion of other possible factors, a comprehensive dental examination must be undertaken to determine whether intradental, periapical, or periodontal lesions may exist. At the conclusion of his examination, the dentist can present his opinion on the possibility of mandibular dysfunction.

Treatment

It appears that the most important problem of our deliberations is to determine which mandibular position, or range of positions, is best for our patients. We must utilize all diagnostic dental techniques and proceed along certain definite lines.

First, we must correct the occlusion by eliminating premature contacts or other traumatogenic factors if they are considered to be a possible cause of the mandibular dysfunction.

Next, the patient should be relieved of pain as soon as possible. Generally, the pain seen in these cases is due to muscle spasm and definite trigger areas can be palpated. These areas are sprayed with ethyl chloride.[26] We may also inject isotonic saline solution or a local anesthetic solution into the muscle.[27] A Luer-Lock syringe with a 21-gauge needle is used so that it is possible to aspirate before injecting.

Since the vast majority of the patients presenting painful head and neck symptoms (without otolaryngologic disorders) have malocclusions, temporary mandibular occlusal splints in conjunction with myofunctional therapy[28] have to be instituted. Not only will the vertical dimension between the jaws change, but the mandible will be capable of shifting to the right or to the left, of rotating to the right or to the left, of tilting in the horizontal and vertical planes, and of retruding or protruding in the sagittal line.

Whenever the occlusal dysharmonies have developed over a period of many years, it can be readily understood that certain degenerative changes may have occurred in the musculature. These range from fibrosis to contracture, and there are concomitant changes in habit patterns. In order to restore the patient to normal, new habit patterns have to be established. It is endeavored to return the patients to what we believe is their normal unstrained mandibular position. However, degenerative changes in the musculature and in the joints will, of necessity, alter our course. Time, therefore, is an essential factor in the solution of the problem.

After cessation of symptoms, and when the patient has been comfortable for several months without evidence of further periodontal breakdown, the permanent restoration of his masticatory function can be undertaken.

Comment on Findings

Tables 1 and 2 show the results of our observation of 100 cases during the past year. The most frequent areas of pain were the internal pterygoid muscles and the temporomandibular joints. However, pain was found in other areas remote from the jaw region. Patients were rendered symptom-free or showed marked improvement by the administering of ethyl chloride spray or procaine injections to those "trigger areas" in the muscle where there was spasm. Frequently, by injection into the internal pterygoid muscles there would be relief of tenderness and pain in the other affected muscles. Favorable results were obtained in some cases simply by correcting the occlusion by means of equilibration or by temporary acrylic splints with adjunctive myofunctional therapy. Other cases required a combination of both procedures. Seventy per cent of the cases seen were of the painful variety. The ratio of females in this group was 3.5:1. This agrees with previous observations.[13]

TABLE 1.—*The Results of Observations of One Hundred Cases During the Past Year*

Symptoms	Observations, No.	Disposition				Results			
		Referred to Own Dentist for Treatment	Mandibular Occlusal Plastic Splints	Equilibration of Occlusion	Ethyl Chloride Spray and/or Procaine Inject.	Not Known	No Improvement	Improvement	Symptom-Free
A. Painful									
Trigeminal neuralgia	1	1				1			
Occipital pain	3	2	1			3			
Facial pain	8	6		2		7	1		
Headaches	10	8	2	1		8			2
Muscle spasms	68	27	8	3	43	25	1	28	14
Cervical pain	2				1	1		1	
Temporomandibular joint pain	44	27	6	2	11	29	1	7	7
Earache	13	9	2			11	1		1
Trismus	2					2			
B. Nonpainful									
Tinnitus	27	16	11			15	6	2	4
Vertigo	5	3	3			3		1	1
Clicking joint	6	4	1			4		1	1
Crepitus in joint	6	6				6			
Bruxism	8	7				7		1	

TABLE 2.—*The Frequency of Spasm in the Muscles of the Head and Neck*

Internal pterygoids	48
Masseters	30
Temporals	22
Sternomastoids	11
External pterygoids	6
Posterior cervicals	6
Digastrics	5

Although only eight cases of bruxism were reported, many of the other patients either clenched, ground, or gnashed their teeth. A majority of the patients in this study were found to be unduly emotionally tense or upset.

Twenty-five per cent of the cases seen complained of subjective ear noises. Correction of the jaw relationships by means of temporary acrylic splints was the method of treatment. The results obtained were of a subjective nature only and showed that one half of those persons selected for treatment noticed some improvement or were symptom-free. Future studies of this problem and of conductive hearing loss that may be related to jaw positioning [25,29,30] will be carried out with due scientific control.

We concur with the findings of Schwartz [12] in finding that Costen's syndrome does not occur uniformly in temporomandibular joint dysfunction cases. The various symptoms of this syndrome can occur either singly or in groups in those cases which were seen at the clinic.

Whenever possible, patients who had their own dentists were referred to them for the construction of partial dentures or full dentures, rebasing of dentures, and resetting of teeth. This accounts for the large number of cases in the "not known" category at this time.

Report of Typical Cases

CASE 1.—A 35-year-old white woman was seen at the clinic in May, 1958. She complained of pain of one year's duration in both temple areas; pain in both temporomandibular joints; pain in both sternomastoid muscles (near their origin); pain in the right and left pterygoid muscles, and headaches every second day in the frontal and temporal regions. Medical and otolaryngologic findings were negative.

Upon dental examination, occlusal disharmonies were evident owing to malpositioned teeth. A temporary acrylic splint was inserted early in June, 1958, to correct the malocclusion. The right and left temporalis muscles and both temporomandibular joints were sprayed with ethyl chloride, and lidocaine (Xylocaine) was injected into the other affected muscles whenever necessary during the course of treatment. The patient was symptom-free by the end of August, 1958, and remains so to date.

CASE 2.—A 34-year-old white man presented himself to the clinic in May, 1958. He complained of pain since November, 1957, surrounding the left ear, which radiated into the mandible and to the upper lip. Most of the left side of his face was painful. The patient had infraorbital and frontal headaches which radiated to the vertex and down the back of the neck. He also complained of tinnitus in the left ear. His hearing was found to be normal. Marked trismus was noted, most probably precipitated by excessive clenching and bruxing. Medical and otolaryngologic examination showed no organic pathology.

The dental diagnosis revealed a case of marked anterior overbite, collapsed posterior occlusion due to missing first molar teeth in the mandibular right and left quadrants, and resultant muscle spasms. The painful muscles were either sprayed with ethyl or given injections with lidocaine. A splint was inserted on May 14, 1958, and within two weeks the patient was feeling much better. He was also instructed to exercise his jaw muscles by passively and actively opening his mouth. Several times during the next few months symptoms reappeared, but with much less intensity. It was not until the end of September, 1958, when he also changed his job, that the patient felt completely fit.

CASE 3.—A 41-year-old white woman was seen late in November, 1958. She complained of tinnitus in the left ear and dizziness, which she first noticed in May, 1958, and which had lasted for one month. Symptoms reappeared again at the beginning of November, 1958, and occurred every day. She had pain in the left temporomandibular joint, in the left internal pterygoid muscle, behind the posterior border of the ramus of the mandible on the left, and in the posterior cervical muscles. Her hearing was found to be normal, and no organic pathology was noted on examination.

Dental examination disclosed missing teeth in the mandibular right and left quadrants, and the patient had been wearing an upper partial denture for 17 years. The lower teeth had been missing for 15 years, and the upper teeth had been missing for a somewhat longer period. The collapsed bite was corrected by means of a temporary acrylic mandibular splint which was inserted

Dec. 17, 1958. The left temporomandibular joint was sprayed with ethyl chloride. The patient was symptom-free five days later. She was able to return to work and travel by subway without a companion and without getting dizzy.

CASE 4.—A 40-year-old white woman was seen at the clinic in November, 1958. She had pain of one year's duration in both temporomandibular joints (the left one more so), both internal pterygoid muscles, both masseter muscles, both temporalis muscles, the left external pterygoid muscle, the left sternomastoid muscle, and the posterior cervicals on the left side. The pain also radiated supraorbitally from the temple regions, resembling a headache. She also complained of an ache in the eyes.

The patient was without all four first molar teeth in the maxilla and mandible, which resulted in a collapsed bite. A temporary splint was inserted on Dec. 15, 1958, to correct the malocclusion. The patient was symptom-free two weeks later.

CASE 5.—A 22-year-old white woman presented herself to the clinic at the end of October, 1958. Her chief complaint was a pulsating tinnitus in the left ear and a marked noticeable clicking in the left temporomandibular joint. Her hearing was found normal. She had an ovarian cyst operation a year before with intubation anesthesia. At the time of examination she was in excellent health.

Dental examination revealed a mandible which was rotated to the left and marked deviation of the mandible upon opening the mouth. A splint was inserted early in November, 1958, to correct the rotation. The click disappeared, but the tinnitus is still present.

Summary

During the past year, observations were made at the New York Eye and Ear Infirmary of 100 cases of otolaryngoiogical symptoms of dental origin. The majority of these patients complained of pain in the head and neck region, which was traced, for the most part, to certain "trigger areas" in the muscles of mastication. The commonest sites for this pain were the temporomandibular joints and the internal pterygoid muscles.

Treatment of these cases was focused on physiological prosthetic management of maxillomandibular dysfunction. A high percentage of successfully treated cases was obtained with this method.

218 Second Ave. (3).

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Suppurations of the Neck

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Although the antibiotic era has lessened the incidence and improved the prognosis of neck suppurations, surgical drainage remains the definitive method of treatment.

In 1941, Weintraub[1] divided the retropharyngeal area into five separate spaces, namely, the paired right and left prevertebral spaces, the paired right and left peripharyngeal spaces, and, lying between the latter two, the unpaired postvisceral space. Infection in the postvisceral space may descend without any interfering barrier into the mediastinum, but infection in the prevertebral and peripharyngeal spaces is not likely to descend into the mediastinum.

I. Postvisceral Space

This space is located between the buccopharyngeal and the prevertebral fasciae and communicates freely with the posterior mediastinum. Furstenberg[2] describes a simple technique to drain this space and the mediastinum: An incision is made along the anterior border of the sternomastoid muscle to the suprasternal notch. The structures of the carotid sheath are pulled laterally and a drain placed into the posterior mediastinum. (One of us, R. C. K., used this approach on two occasions and, in each instance, was impressed with the simplicity of the procedure.) The postvisceral space also can be approached higher in the neck through the submaxillary fossa.

CASE 1.—An acutely ill 3-week-old infant was brought into the office because of submaxillary swelling and slight elevation of temperature. Therapy with penicillin, erythromycin (Ilotycin) and chloramphenicol (Chloromycetin) was begun. A radiogram showed the larynx and trachea displaced anteriorly by a large post-visceral-space abscess with mediastinal extension. Under local anesthesia, a liberal horizontal incision was made in the submaxillary area and a finger was passed without difficulty beneath the submaxillary gland into the postvisceral space; 40 cc. of pus was evacuated. The child's condition was critical for

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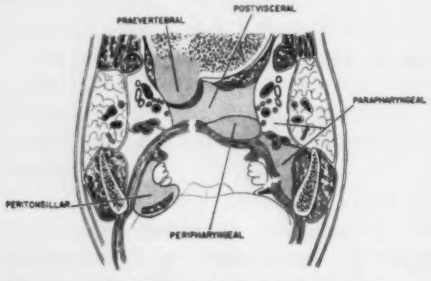


Fig. 1.—The relationship of the pharyngeal space abscesses to the normal structures. Reproduced with permission from Tschiassny, K.: *Cincinnati J. Med.* 26:337, 1945; Cincinnati.

Fig. 2.—Demonstration of a postvisceral space abscess which has caused swelling in the submaxillary area.

Fig. 3.—X-ray demonstrating the increase in the space between the tracheal air column and the vertebral column, which indicates a postvisceral space abscess, in a 3-week-old infant (see Fig. 2).

24 hours following the procedure, owing to respiratory obstruction, necessitating stimulants. The drainage from the neck subsided in six days, but a swelling appeared in the area of the last two ribs, posteriorly, on the left. X-ray studies showed osteomyelitis involving these two ribs; however, at time of discharge from the hospital, the swelling had disappeared. During the sixth hospital week, the child was taken from our care by the parents. Recent information from the family physician revealed the patient to be well.

II. Peripharyngeal Space

The peripharyngeal space (Fig. 1) is formed by a duplication of the buccopharyngeal fascia. In our experience, this is the most commonly involved space in infants. Suppurations in this space remain lateralized and localized, extending from the level of the nasopharynx to the cricoid, and do not extend into the mediastinum. Tschiassny[3] states that the abscess is caused by a suppurative buccopharyngeal lymphadenitis. The lymph nodes are arranged in medial and lateral groups, the medial node usually disappearing during the first year of life, thus explaining why this suppuration is seldom seen after the age of one year.

CASE 2.—A 7-month-old boy was admitted to the hospital at 3:40 p.m. in respiratory distress. At 9:30 p.m. the pediatric resident placed an endotracheal tube near the larynx, maintaining an airway until a tracheotomy could be done. Examination following tracheotomy showed a large swelling on the left side of the oropharynx, which was recognized as a peripharyngeal abscess. The abscess was opened through the mouth with the child in the head-low position, and Escherichia coli was cultured from the pus. It is certain that the child would have drowned in the large amount of pus removed from this abscess had it ruptured spontaneously. Treatment consisted of 100 mg. of streptomycin every 12 hours and 200,000 units of procaine penicillin every 6 hours. The following day the child was much improved. X-rays taken at this time showed only questionable thickening in the retropharyngeal area. The tracheotomy tube was removed on the third hospital day, and the patient was discharged on the seventh day as cured.

III. Prevertebral Space

This space (Fig. 1) lies between the vertebrae and the prevertebral fascia and is not the same as the postvisceral or the peripharyngeal space. An abscess in the prevertebral space is usually caused by cervical vertebral tuberculosis. Suppuration is not likely to extend into the mediastinum but may descend into the supraclavicular or axillary fossa. We feel this to be a rare suppuration and have not encountered this type of abscess in our experience.

IV. Peritonsillar Space

The commonest suppuration (Fig. 1) involving the juxtapharyngeal spaces is the familiar peritonsillar abscess located between the fascia covering the pharynx, the anterior and posterior pillars of the tonsil, and the tonsil. This type of abscess occurs rarely in the very young but commonly after puberty. The youngest patient seen in our experience with such an abscess was a 10-year-old girl. Fatal complications can occur as a consequence of peritonsillar abscess, e.g., hemorrhage, jugular vein thrombosis, and edema of the larynx with spread to other spaces.

V. Parapharyngeal Space

The parapharyngeal space (Fig. 1) was called the pharyngomaxillary fossa by Mosher.[4] Quoting liberally from this author, the space may be described as being bounded medially by the superior constrictor muscle with the attached tonsil. The boundary below is the internal ptyergoid muscle lining the inner surface of the ascending ramus of the jaw and complementing the masseter on the outside. The outer boundary above is the parotid gland. The fossa is bound by the prevertebral muscles and prevertebral fasciae. The fossa is divided into unequal parts by the styloid process and the muscles arising from it. The space formed may be considered a cone, the base of which is attached to the base of the skull around the jugular foramen. The apex of the cone is at the hyoid bone, the carotid sheath emerging from the apex of the cone. For practical purposes, the sheath may extend the continuity of the fossa, through the neck, and into the thorax.

The tonsil is the commonest source of infection involving this space. Infection may also enter the space from the parotid gland, from the mastoid (Bezold's abscess), from a thrombosis of the jugular vein, or from extension of infection from other spaces. Mosher suggested that the space be drained through the submaxillary fossa using a large T-shaped incision.

CASE 3.—A 53-year-old white, mildly diabetic woman was admitted to the hospital in severe respiratory distress. An emergency tracheotomy was done and the patient placed on prednisolone acetate (Sterane), crystalline trypsin (Parenzyme), sulfisoxazole (Gantrisin), erythromycin, and chloramphenicol. Her illness had begun with a sore throat two days before admission, for which her family physician prescribed chloramphenicol. At the time of admission to the hospital, the entire left side of the patient's neck was indurated from the ramus of the jaw to the clavicle and from the trapezius muscle to the medial line of the neck. The left tonsil was deviated toward the median line. On the fourth hospital day, an extensive incision was made parallel to the ramus of the jaw, extending from the anterior border of the trapezius almost to the median line of the neck. A finger was passed through the submaxillary fossa into the parapharyngeal space and foul-smelling pus gushed from the wound. Staphylococcus pyogenes var. albus and E. coli, both sensitive to nitrofurdantoin (Furadantin), neomycin, and polymyxin B, were

Fig. 4.—X-ray taken immediately after surgery (fourth hospital day), showing a large mediastinal abscess which subsequently was drained through a submaxillary fossa incision.

Fig. 5.—X-ray taken on the 26th hospital day, showing the mediastinal abscess resolved but a pericardial fluid level (see arrows) present (see Fig. 4).

Figure 4

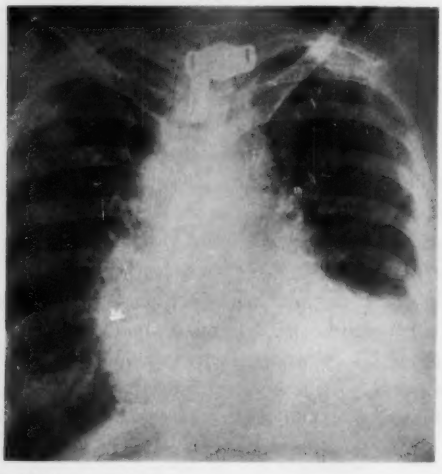
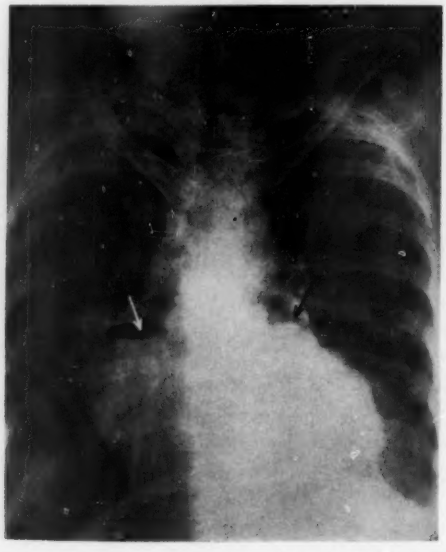


Figure 5



cultured. After surgery, radiologic examination showed a huge mediastinal abscess, which ruptured into a bronchus on the sixth postoperative day, causing severe respiratory distress. On the 13th hospital day the patient was near death. Nitrofurdantoin (in 500 cc. of 5% dextrose) was given intravenously in doses of 180 mg. b.i.d. for 7 days; in doses of 50 mg. every 6 hours for 2 days, and, finally, every 12 hours for 5 days. Improvement was prompt. Drainage from the neck and bronchus continued until the 26th postoperative day. The following day, 30 cc. of sterile sanguineous pericardial fluid was removed. The patient was discharged from the hospital on the 34th hospital day. When last seen, there were no sequelae from the drugs, the treatment, or the disease.

VI. Ludwig's Angina

Although everyone is familiar with Ludwig's angina, few know the nature of the disease. Tschiassny [5] employed the term "pseudo-Ludwig's" to designate forms of suppurative submaxillary lymphadenitis enlarging in the direction of the mouth and isolated cellulitis in either the sublingual or the submaxillary space. Tschiassny [6] uses the following criteria to differentiate "pseudo-Ludwig's" from "Ludwig's angina":

1. Ludwig's angina is a cellulitis, not an abscess.
2. It starts regularly in the submandibular space —not in the sublingual space.
3. It involves both spaces, usually bilaterally—never one single space.
4. It produces gangrene with a serosanguineous putrid infiltration but very little and even no frank pus.
5. It attacks the connective tissues, fasciae, and muscles—not the glandular structures.
6. It spreads by continuity—not by the lymphatics.

CASE 4.—A 60-year-old mildly diabetic Negro man was admitted to the hospital on June 14, 1958, and discharged 12 days later. Four days before admission, the left lower molar and premolar teeth were removed. Twenty-four hours after the extractions, the patient received 600,000 units of procaine penicillin and another 600,000 units twenty-four hours before admission because of massive swelling which began in the left submaxillary area. When seen by one of us, the swelling had extended into the sublingual space and involved both sides of the neck. The tongue protruded into the mouth toward the palate. Chloramphenicol, 500 mg. every 8 hours, intramuscularly, and 2,000,000 units of crystalline penicillin in 1,000 cc. of saline were given intravenously. A triple sulfonamide compound was given orally.

Twelve hours after admission, under local anesthesia, a large U-shaped incision was made from one submaxillary area to the other. The mylohyoid muscles were cut through, but an effort was made to save the anterior bellies of the digastric muscles. Less than 2 cc. of pus was found in the area about the left mandible. S. pyogenes var. albus, sensitive to penicillin and Panalba, (tetracycline phosphate complex and novobiocin) was cultured. The swelling was almost entirely due to a cellulitis. The temperature dropped from 101 F to normal in 24 hours following surgery, and recovery was rapid.

Summary and Conclusions

The cases reported illustrate the importance of determining which space is involved when planning the surgical approach for incision and drainage of an abscess. Peritonsillar and peripharyngeal suppurations are opened through the mouth. Parapharyngeal, postvisceral, prevertebral, and Ludwig's angina should be approached externally.

In Cases 1 and 3, the patients developed mediastinal abscesses as complications of the neck suppurations. In each case, the suppuration was drained through the submaxillary fossa. Osteomyelitis of the ribs and pericardial effusion were two unusual complications occurring in cases of neck suppurations.

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The Role of the Nasofrontal Suture in Rhinoplasty

Hump Removal Simplified

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No references are found in rhinoplastic literature to the importance of the suture line between the nasal process of the frontal bone and the cephalic borders of the nasal bone and of the frontal process of the maxilla. This natural-cleavage line automatically delimits all surgery on the upper part of the bony dorsum or bridge. This synarthrosis, or suture, is finely serrated. In older persons, the suture may be almost completely fused, but there always remains the external weak line which aids disarticulation. In the young adult, there is often a fine layer of periosteum separating the adjacent bones, making it still easier to disarticulate. Knowledge of this area has made it possible to develop an extremely simple technique which greatly facilitates surgery on the bony nasal dorsum.

Anatomy

A few pertinent facts will be sufficient. The nasofrontal suture is slightly above the level of the transverse center of the orbits and is high in the center and runs caudally, laterally, and posteriorly to join the frontolacrimal suture (Fig. 1). Above the suture, the notched nasal process of the frontal bone may be solid or may be excavated by the frontal sinus or an ethmoid or agger cell. Nasal bones vary in size and shape. Rarely, there may be agenesis of the nasal bones (their place being taken by the nasal process of the maxilla), or the perpendicular plate of the ethmoid may project between the nasal bones. The average thickness of the upper edge of the nasal bone is less than one-fourth of an inch, variations depending on the curve of the bone and the presence of the frontal spine and sinus. The posterior surface of the upper part of the nasal bone lies on the caudally projected frontal spine, where it fuses with the perpendicular plate of the ethmoid (Fig. 2 and 3).

Luongo and Luongo recently gave an excellent description of the region of the nasion, but this description makes no reference to the value of the suture line as an aid in surgery. It states:

> If to complete an osteotomy a chisel is used to fracture at the masion, the surgeon should bear in mind that this technique may cause fracture of the sloping edges of the nasal notch, of the frontal spine, of the perpendicular plate of the ethmoid, destroying the main support of the nasal bridge, and the impact of the chisel may even be transmitted to the cribriform plate; furthermore,

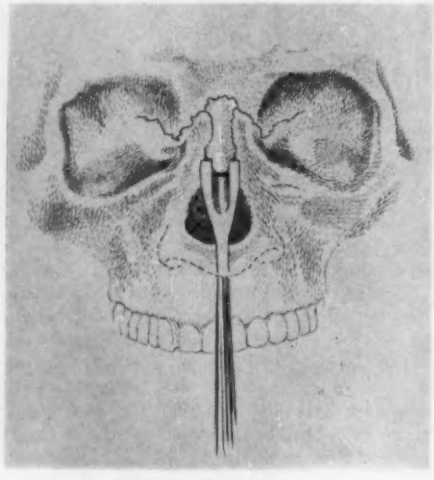

Fig. 1.—External anatomy of nasofrontal suture showing an unusually small nasal bone. The hump gouge has already engaged the lower edge of bony bridge. The wings of gouge straddle the dorsum and can be felt through the skin.

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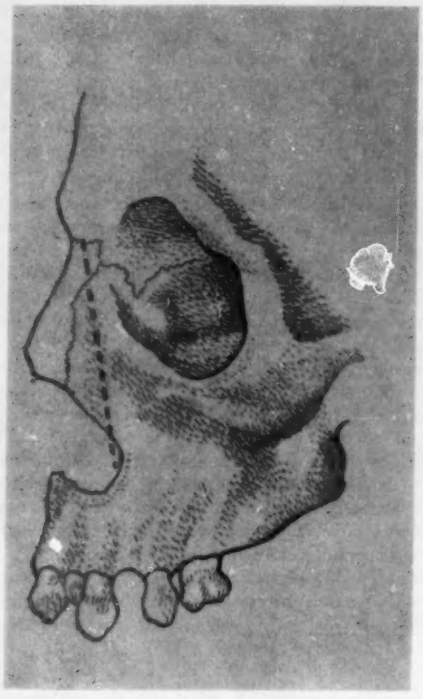


Fig. 2.—Lateral-external view of nasofrontal suture with dotted line to indicate osteotomy.

Fig. 3.—Internal view of nasofrontal suture, showing nasal bone resting on frontal spine as well as line of osteotomy to facilitate disarticulation.

when the frontal sinus extends below the frontonasal suture line which is located at the nasion, the chisel may force the ends of the fractured bones into the lumen of the sinus, causing frontal sinusitis.

All these possibilities are avoided in this disarticulation technique because no chisel is used to complete the osteotomy. Further, the authors say:

This type of construction makes infracturing difficult and inadvisable. Outfracturing is the procedure to be chosen.

Goal

My goal was, *A*, to remove in one piece, with the least trauma to the periosteum on the outside and to the soft tissues on the inside of the nose, a central wedge of the

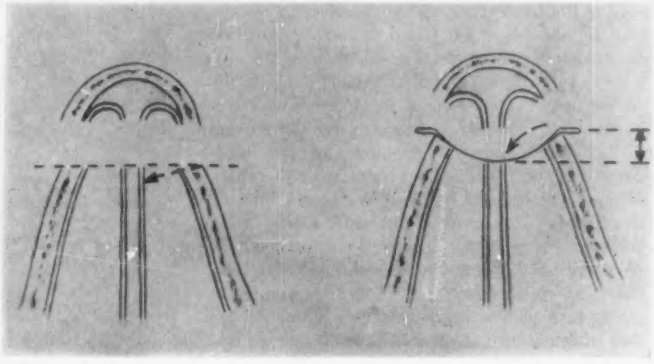


Fig. 4.—End-result when hump is removed by saw or chisel as compared with hump gouge.

bony dorsum which would include (1) nasal bones, (2) part of the solid angle which is the upper thickened end of the nasal bone, and (3) the septum which is simultaneously cut at a lower level than (Fig. 4) the lateral walls. (This can generally be done in one sweep of the hump gouge.); *B*, to do the lateral osteotomies with one simple osteotome and without elevating the periosteum in such a way that the entire lateral mass of nasal bone and nasal process of the maxilla would be separated and disarticulated in one piece, without comminution of bone, deposition of bone-dust, or laceration of intranasal mucosa. (This should leave a smooth, narrow bony dorsum without an "open roof.")

Anesthesia

A few drops of equal parts of cocaine, 10%, and epinephrine are sprayed into the nose, and the mucous membrane is rapidly swabbed three times with the same. I have never packed a nose with anesthetic solution. I get absolute anesthesia by direct application without dripping and excessive absorption. Then I inject procaine hydrochloride (Novocain), seldom more than 10 cc., sparingly, in the operative area. I have not felt any need to use hyaluronidase. I do not balloon the tissues.

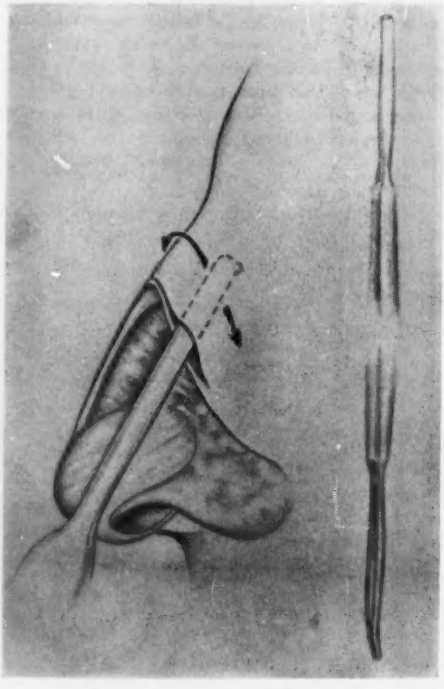
Technique

The usual incisions are made with only one knife, a No. 15 blade.

Then the periosteum is elevated in one sheath with a double-end elevator. I begin by making an incision with the sharp lip of the shorter end in the periosteum on the patient's left, just above the edge of the nasal bone. Then the elevator sweeps laterally and mesially to elevate a complete hood of periosteum, subcutaneous tissue, and skin (Fig. 5). I do not jab upward which definitely shreds the periosteum. I then reverse the instrument (with its compound curves) and sweep over the dorsum to partially elevate the opposite side and come down over the cartilaginous vault with the sharp section. The opposite side is then elevated with the short end. This method prevents shreds from bunching up or from dipping down between the separated nasal bones. The smooth hood effectively covers all rough edges of the bones. If our teaching is correct, that periosteum aids in the deposition of bone, then we should preserve all we can. It has been argued that unnecessary thickness of the soft tissues over the bony dorsum will result unless we remove the periosteum with the hump. This has never occurred since I began elevating the periosteum in one sheath. Although there are no elastic fibers in the periosteum, experience has shown that it will shrink to adapt itself to the smaller framework (Fig. 6).

I now cut the attachment of the upper lateral cartilaginous wing from the septal cartilage and, with the same angulated scissors, remove a section of the ventral edge of the septal cartilage to reduce the projection. This permits me to place my gouge against the thin edge of the nasal bones and, with a few taps of the mallet, the hump is removed (Fig. 7). This piece of bone separates readily at the suture line if it is rocked from side to side after the gouge has nearly completed the cut to the upper edge of the nasal bone. The wings of the gouge are easily felt under the skin to guide this maneuver. If the hump is small or moderate, the gouge engages the edge of the nasal bones rather superficially. If the hump is large, it is placed deeper, and then small wedges may be chipped off the mesial edges of the nasal bones; this is rarely necessary. The subglabellar dip or

Fig. 5.—Incision of periosteum near edge of nasal bones permits lateral and mesial elevation without shredding.



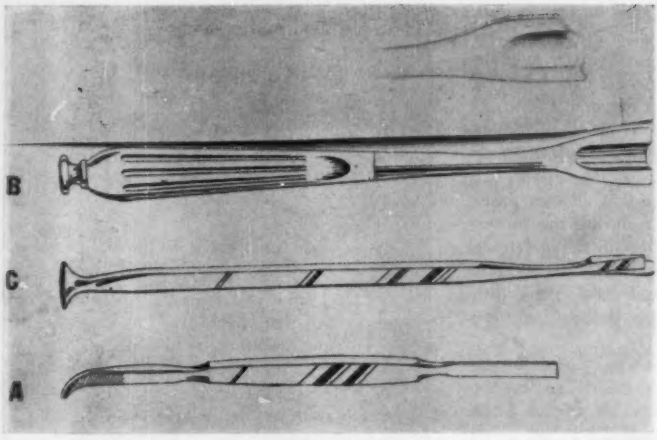


Fig. 6.—(*A*) Periosteal elevator at one end makes incision and permits side to side elevation. Other end is blunt, curved, with sharp edge to cut fibrous bands over dorsum. (*B*) Hump gouge (rocking gouge). The cutting edge is confined to the curved depression. The wings are dull and can be felt under the skin for guidance. (*C*) Osteotome (small wedge) permits changing direction of cut. Lip elevates and guides direction of cut.

nasofrontal angle may be deepened if needed. If an implant is to be used to build up a saddle deformity, the gutter created by the hump gouge makes an excellent bed.

The next step is very important. A straight 7 mm. osteotome is passed along both sides of the septum to further separate the remains of the thick upper part of the nasal bones from the perpendicular plate. Then a thin rasp bevels the ental edges of the septum and nasal bones to remove the mucoperiosteum and bone which may interfere with bony union when the nasal bones are approximated after the osteotomies.

The lateral osteotomies are done through the usual incisions. I do not elevate the periosteum. The protective lip on my osteotome, just ahead of the cutting edge, separates the soft tissues with much less trauma. The osteotome straddles the thin edge of the pyriform crest and is first tapped toward the occiput to get a purchase, then swung into the correct position toward the nasofrontal suture. It does not cut completely through the upper thick edge of the frontal process of the maxilla or nasal bone. It creates a green-stick fracture. Hence, it does not cut or lacerate the mucoperiosteum on the inside of the nose where there are large vessels, nor does it permit the lateral walls to be displaced and lost. As it approaches the suture, the wedge-shaped blade separates the bones so that the whole lateral nasal bony wall is disarticulated without comminution, and no force or rocking is needed. There is neither outfracture nor infracture, nor is there any necessity for the use of a chisel at the nasion to complete the osteotomy, nor for a Walsham forceps to sever bony union. No dust accumulates between the cut edges. This should definitely discourage bony regeneration and broadening of the nasal base. This lateral wall, as if loosely hinged at the frontal suture line, can, if necessary, be impressed under the cut edges of the maxilla. This should be done in broad noses, after removing a *minimum* of the dorsum.

Now the profile line is straightened and the cartilaginous vault treated as necessary. Where the

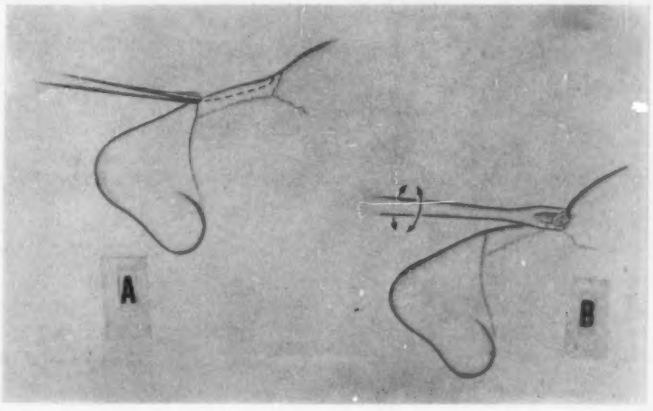


Fig. 7.—(*A*) Placing gouge at end of bony nasal bridge. The line of bone incision can be easily varied from straight to curved. (*B*) Shows how gouge is rotated to disarticulate or excavate.

septum is markedly deformed, and most of it must be removed, pieces may be placed in the gutter created by the hump gouge to prevent saddling. The intact hood of periosteum and skin holds the fragments in contact with the remaining bone. In deviated noses, the gouge can be placed off center, i.e., lateral to midline so as to equalize both lateral walls.

It is important to emphasize that, in some cases, the bony dorsum may retract during the process of healing. The cartilaginous vault never retracts if the septum is intact. Therefore, after the profile line has been straightened, take off a little extra of the septal cartilage as well as the upper and lower laterals.

This technique is basic for all types of deformity of the bony bridge. From a strictly engineering viewpoint, the solid angle must be reduced in all cases in order to present a parallel-walled gutter with a lowered septum. This will permit the lateral nasal walls to meet each other at the apex of the dorsal triangle. With most techniques, the removal of the hump results in an oval-shaped gap; the septum and lateral walls are on one plane and very little, if any, of the solid angle is removed. (Fig. 8) One cannot expect to get a straight line by bringing two concave lines in apposition, especially with the septum in between. But, if we have two parallel edges brought into contact by moving the lateral walls toward each other, and if we eliminate the septum and all soft tissues from preventing contact of bone to bone, we should get a better bony union.

Anderson and Rubin have recently described an interesting approach to surgery of the bony dorsum. They not only elevate the external periosteum but also the mucosa under the bone and cartilage as well as that of the upper part of the septum. This creates a submucosal tunnel for the use of the Neivert Gouge. They state there is less trauma and, therefore, less bleeding and swelling. While their approach is different, the work on the dorsum is more or less similar.

They state that this method of hump removal

> . . . is less traumatic than the usual saw type, because only a few light taps of a mallet are needed and since the force is applied in a straight line, there is no problem of lateral vibration and no need to take vigorous measures to steady the head. Such lateral vibration and repetitive stretching of the tissue as a result of the excursions of the saw is definitely traumatic and contributes in large measure to post-operative edema and hematoma.

Furthermore, Anderson and Rubin state:

> To master the use of the saw, one must train and perfect his movements much as a golfer must practice stance, grip, and swing; not holding the elbow at the proper height, failing to deliver the force through the shoulder, or allowing the plane of the saw cut to become angulated will prejudice results. In this method, all that is required is to be able to direct a straight instrument along a straight line with the added help of being able to follow the progress of said instrument with the finger as well as the eye. Thus, it is much easier to teach this type of hump removal than it is to teach removal with the saw, and the student invariably approaches it with a great deal more confidence of success.

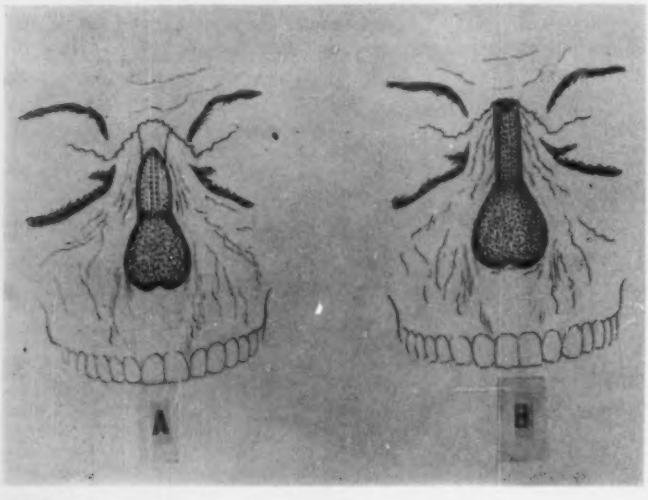


Fig. 8.—(*A*) Oval defect resulting after use of saw or flat chisel. (*B*) Parallel-walled excavation, including septum and upper end of thick nasal bone when hump gouge is used.

Fig. 9.—One-blade nasal speculum, useful for all nasal surgery and as a dorsal elevator and packing forceps.

If the nasofrontal angle is shallow, it is generally recommended that deepening be done, before the hump is removed by the saw. This is technically very difficult, time-consuming and laborious; when the technique outlined above is employed, the angle is treated as part of the hump and is easily, quickly and completely removed with little extra effort.

Dressing and Aftercare

After the petrolatum packing is placed (Fig. 9), it is my custom to cover the nose with the usual adhesive strips, leaving some of the tip exposed. Then I apply a previously shaped stiff copper splint lined with lint and strap it in place. This can be compressed medially to keep the nose narrowed. On top of this I apply stent extending over the forehead to prevent lateral displacement. On the third day packing and dressing are removed, and the patient leaves the hospital on the fourth day without any dressing or packing.

To reduce postoperative edema, on the morning after operation I generally order one intramuscular injection of 2 cc. meralluride (Mercuhydrin). In most cases the edema disappears in less than 48 hours. Chlorothiazide (Diuril), an oral preparation, can be given, two 50-mg. tablets, hydrochlorothiazide. Only one dose of either drug is needed. Lately, I have tried buccal streptokinase-streptodornase (Varidase) in addition. This will liquefy the exudate of blood and tissue elements so that the swelling becomes more amenable to drainage by the meralluride or hydrochlorothiazide. Beginning three hours after surgery, one tablet is allowed to dissolve in the buccal pouch four times a day for three days.

On the 10th day, I begin to massage any swelling and apply my self-adjusting splint for 15 minutes at a time to stretch the developing callus (Fig. 10). The lateral osteotomy gap cannot remain a vacuum. Therefore, either it must fill in with callus or the severed bones must reunite. Generally, after an osteotome is used, a fibrous union develops which can be stretched for a long time. This, to a great extent, prevents broadening of the bony bridge. When a saw is used some of the sawdust remains, helping to form bony union and reattachment with broadening.

Fig. 10.—Self-adjusting nasal splint.

Fig. 11.—My first case done by disarticulation (1948).

Conclusion

Knowledge of the anatomy of the nasofrontal suture and its environs gives us information of the natural lines of cleavage in surgery of the bony dorsum. Operative procedures based on this knowledge, with instruments designed to take advantage of the architecture of this region, make it easier and quicker to get good results with less trauma, less edema, less bleeding, and a shorter healing period (Fig. 11).

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Transmeatal Condylectomy and Meniscectomy

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The surgical approaches to the temporomandibular joint have often been complicated by injury to the temporal branch of the facial nerve as well as by lines of incision which require much soft tissue dissection and retraction in order to obtain a satisfactory degree of exposure. The resulting motor weakness and facial scarring has made it desirable to design other methods for operating on the condyle and meniscus.

The first description of a transmeatal approach to this problem was given by Davidson,[1] in which the anatomical feasibility of approaching the temporomandibular joint through the junction of the superior and anterior wall of the ear canal was outlined. This approach was used by Davidson for five cases of condylectomy, three cases of meniscectomy, and one case of bilateral resection of the condyle and mandibular neck for bony ankylosis of the jaw. We have modified the original operation in five recent cases and again delineate the procedure by means of concise surgical anatomy.

Indications

The most frequent indication for exposure of the temporomandibular space occurs in persistent displacement of the articular disc. The dislocation may occur during a "whiplash" injury of the head when the mouth is open. The usual history is one of an automobile accident in which the injured occupant is talking when the vehicle is suddenly and forcibly halted, snapping the head forward in a whip-like fashion. The subsequent mandibular displacement is described by the injured person as a sudden "click," or "heavy sensation," in one or both temporomandibular areas, followed by increasing pain in these areas during mastication. Spontaneous or delayed trismus is common, with or without an audible click in the involved joint.

The symptoms may be explained by a combination of events. Following the injury, the posterior thinned-out portion of the articular disc becomes detached from the capsule and is drawn upward and forward by the external pterygoid muscle. Thereafter, as the mouth closes by elevation of the jaw, the pathological disc is crushed between the condyle and the glenoid fossa and gradually becomes atrophied and scarred. The immediate trauma is also responsible for hematomas into the joint. These may persist for months, causing further reaction and loss of function in the articulation. The articular disc displacement, scarring, and hematomas, alone or in combination, seem sufficient to explain the clicking, pain, and trismus.

Accordingly, the surgical exposure of the joint must be designed to fully visualize the disc, the glenoid fossa, the condyle, and the spatial relationships of these structures, in order to correctly diagnose and treat the specific pathology. The pain pattern with temporomandibular malfunction is usually referred to the pinna, suggesting the auriculotemporal nerve as the sensory pathway. It would seem important that the operation be so designed as to allow sectioning of this nerve during the procedure.

Chronic displacement of the articular disc is also seen from a direct blow to the jaw when the mouth is open. A direct blow may also be responsible for fractures of the mandibular neck and may constitute another

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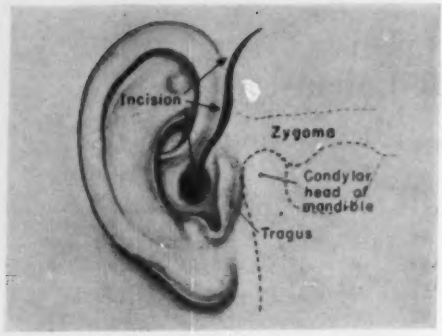


Fig. 1.—Outline of the transmeatal incision.

indication for surgical exposure. The other, less frequent, indications include chronic dislocation, or ankylosis, of the joint. In all of these conditions, direct exposure of the space followed by meniscectomy and/or condylectomy is frequently the treatment of choice.

Operation

The operation is best performed under general anesthesia, which also allows for unrestricted passive movement of the jaw while the joint is exposed. Preoperative preparation of the operative field consists of a thorough cleansing of the external auditory canal of cerumen and shaving the temporal hair to the superior level of the pinna.

After sterile preparation and draping, the incision is outlined in methylene blue and injected with five cubic centimeters of one per cent lidocaine (Xylocaine) containing six drops of 1:1000 epinephrine in one ounce of lidocaine (Fig. 1). The incision is started in the anteroinferior aspect of the external auditory canal and carried superiorly to follow the cleft between the tragus and the helix. It is lengthened superiorly to the level of the attachment of the pinna and then curved gently anteriorly for a distance of two centimeters. The transmeatal portion should divide the cartilaginous canal from the bone of the tympanic plate of the anterior external auditory canal. The extrameatal extension should incise skin and subcutaneous tissue only. Retraction then allows exposure of the superficial temporal branch of the facial nerve, posterior aspect of the zygoma, articular capsule, and a minor portion of the parotid gland (Fig. 2).

The temporal artery and vein are isolated, divided, and ligated. The auriculotemporal nerve is divided. Next, the articular capsule is divided in an anteroposterior direction, permitting direct exposure and inspection of the condylar head and articular disc (Fig. 3). At this point, it is not uncommon to evacuate a small amount of old, un-

Fig. 2.—Surgical exposure of the structures overlying the temporomandibular joint. The dotted line illustrates transverse division of the articular capsule.

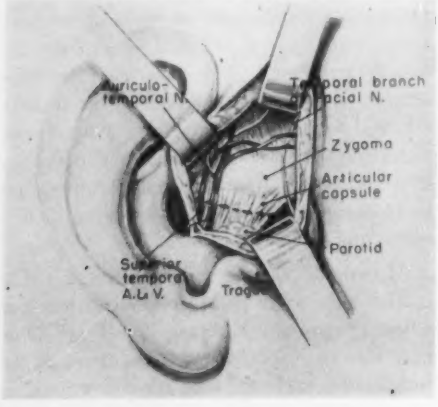
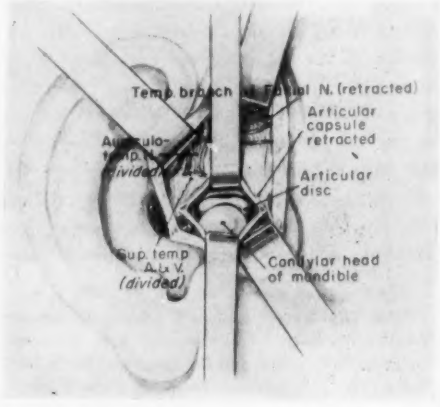


Fig. 3.—Retraction of the articular capsule and exposure of the articular disc and condylar head.



clotted blood from the joint space. Movement of the jaw by the anesthetist will also help evaluate the gross pathology.

Should a meniscectomy be necessary, the articular disc is grasped with a clamp and all attachments are severed under direct visualization. In those cases requiring a condylectomy, the disc is first removed to allow for better exposure and the condyle is excised by transecting the mandibular neck with a bone rongeur or Gigli saw. Bleeding from the pterygoid muscles is always present but can be controlled easily because of the wide exposure. The incision is closed with 00000 Dermalon (skin and tension suture processed from nylon), beginning in the transmeatal portion. A small drain is placed superiorly, and a firm dressing is applied. Patients are not restricted in jaw movement postoperatively and are placed on a soft diet starting the first postoperative day. Sutures are removed on the fifth day after surgery.

Report of Cases

CASE 1.—A 46-year-old white man was involved in an automobile accident sufficiently severe to cause a whiplash movement of his head. He noted an instantaneous onset of pain in both temporomandibular joints, particularly on the right, associated with difficulty in fully opening the mouth. The symptoms became more prominent over a three-month period, and he sought medical attention because of severe pain in the right temporomandibular joint. Examination revealed a right lateral deviation of the jaw during opening and severe pain on palpation over the right condyle and posterior zygoma.

Exposure of the temporomandibular joint on the right was done through a transmeatal route. Immediately upon entering the joint, a cubic centimeter collection of dark, unclotted blood was noted. The disc appeared intact but adherent to the condylar surface of the mandible. The adhesions were cut, and the articular disc was removed.

The postoperative course was marked by a complete remission of the patient's pain upon opening and closing the jaw. He was discharged on the seventh day after surgery, free from complaints.

Comment.—This patient did not demonstrate clicking of the joint but did have severe pain. Evident pathology at operation included a collection of old blood and an adherent meniscus. The rapidity of remission in his pain immediately after anesthetic recovery suggests that section of the auriculotemporal nerve is an important part of the procedure. It would seem probable that surgical trauma in itself should act as a source of pain but lacked a means of referral.

CASE 2.—A 24-year-old white woman sustained a whiplash injury of the head in an automobile accident and immediately felt a "heavy sensation" in both temporomandibular joints. Three days after injury she began to have progressive trismus, pain, and audible clicking in the left joint. Examination revealed inability to fully open the mouth and an audible click on auscultation with a stethoscope over the left temporomandibular joint while opening the mouth.

Operation by transmeatal route six weeks after injury showed two cubic centimeters of dark, unclotted blood in the left temporomandibular space. The articular capsule was adherent and fixed by adhesions to the superior surface of the synovial lining of the condylar portion of the mandible. There was no atrophy of the disc, although it was obviously displaced anteriorly. The pathological disc was removed.

Postoperatively, the trismus gradually disappeared. She had no further complaints of joint pain or clicking.

Comment.—Removing the pathological disc and evacuating the hematoma was sufficient to relieve all of the symptoms. Pain referred to the ear and zygomatic area was absent in this patient. However, the auriculotemporal nerve was sectioned to decrease the possibility of future referred pain and to encourage a postoperative course free from pain.

CASE 3.—A 33-year-old white man sustained direct injury to the left temporomandibular joint in an automobile accident on Dec. 7, 1957. During the accident, the left temporal area of the face was traumatized against the windshield. He immediately felt pain in the left temporomandibular joint, radiating to the pinna of the ear and accentuated by jaw movements. In addition, he began to note a gradual onset of clicking in the involved joint in opening and closing the mouth.

Surgery of the joint by a transmeatal approach was done five months after the injury. There was evidence of unclotted dark blood in the joint space. The meniscus was atrophied and completely adherent to the synovial sheath of the condyle. A meniscectomy was performed with complete remission of symptoms postoperatively.

Comment.—Adhesions, disc atrophy, and hematoma were all present during the operation. Postoperatively, there was immediate and complete freedom from pain in the pinna and joint, probably secondary to complete sectioning of the auriculotemporal nerve during surgery. In this case, the disc was firmly bound to the condyle with adhesions, but, because of the exposure afforded through the transmeatal route, a sharp dissection was easily performed.

CASE 4.—A 35-year-old white woman experienced a whiplash motion of the head following an automobile accident in February, 1958. There were no complaints except some immediate difficulty in opening the mouth. However, this became progressively worse, accompanied by pain in the left temporomandibular joint and the left ear while closing the mouth.

Exposure of the left joint through a transmeatal incision demonstrated a complete fracture of the meniscus with displacement into the anterior portion of the glenoid fossa. There were also firm adhesions between a severely eroded condylar head and the thickened synovial lining of the glenoid fossa. Accordingly, both a meniscectomy and condylectomy were done.

The postoperative course was uncomplicated. There was complete freedom from pain and a gradual return of full jaw motion.

Comment.—Because of the close proximity of the transmeatal incision to the joint, it is particularly easy to visualize the condylar head and meniscus as a unit. The decision to operate on the condyle as well as on the meniscus is simplified. The wide exposure readily permits removal of either the meniscus or the condyle, or both.

CASE 5.—A 34-year-old Negro woman received a direct blow to the symphysis menti in September, 1958, which resulted in a bilateral fracture of the mandibular neck and medial condylar displacement. Symptoms of pain and trismus were prominent.

The left temporomandibular space was easily exposed by a transmeatal technique, revealing a complete fracture of the condyle through the neck with rotation anteriorly and inferiorly. A moderate amount of old, unclotted blood was present. The condyle was grasped, and, under direct visualization, the distal end of the free segment was identified, severed from the external pterygoid muscular attachments, and delivered. The proximal segment of the mandible was then trimmed with a rongeur and the incision closed. An identical procedure was performed on the right side four weeks later.

The postoperative course was uncomplicated. The patient rapidly developed full motion of the jaw without pain.

Comment.—It was felt that removal of the condylar segments with acceptance of bilateral false joints would offer a safe, rapid method of repair. This decision was verified by absence of complications and excellent postoperative function.

Summary

A transmeatal approach to the temporomandibular joint is advocated for a safe, adequate anatomical exposure and effective meniscectomy or condylectomy.

The surgical anatomy of this procedure is delineated and illustrated.

Whiplash injury to the cervical region may be associated with disturbance of temporomandibular function and articular disc injury.

Dr. Edmund P. Fowler Jr., assisted in outlining the surgical approach.

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Fatal Granulomatosis of the Respiratory Tract (Lethal Midline Granuloma-Wegener's Granulomatosis)

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Fatal granulomatosis of the respiratory tract is a disease with a noteworthy natural history, recognizable clinical manifestations, and identifying pathologic characteristics. Men, women, and children of all ages are susceptible, many of whom have no previous stigmata of allergic or vascular disease.

The earliest reference to this disease appeared in 1897, when McBride[1] reported bizarre ulcerative granulomatous lesions in "a case of rapid destruction of the nose and face." Similar cases have been reported by Fordyce,[2] Woods,[3] Falchi,[6] Chatellier,[7] Kraus,[8] Stewart,[13] and others. In 1936 and 1939, Wegener[26,27] published three cases characterized by necrotizing granulomatosis of the nose, nasal accessory sinuses, larynx, and lungs associated with a "peculiar granulomatous nephritis." Wegener believed that the nose was the primary site of the disease and applied the term "rhinogenous granulomatosis" to the disease process.

A review of the available literature from 1897 to 1957 reveals that there are a number of reports of similar cases, often with varied interpretations and diagnoses, suggesting that the protean manifestations of the disease meant many things to different investigators. Nosological impressions, such as lupus nasi,[24] hyperallergic Boeck's disease,[31] a malignant new formation,[41] rheumatoid granulomatosis,[15] atypical lymphosarcoma,[19] and respiratorenal polyarteritis nodosa,[55] indicate the confusion caused by the various descriptions (Table 1).

This work is an attempt to describe the clinical characteristics with illustration of the roentgen features; to illustrate the pathologic-anatomic picture; to report our ob-

TABLE 1.—*The Onomatology Attached to Fatal Granulomatosis of the Respiratory Tract*

Year	Ref.	Diagnosis
1897	1	Rapid destruction of nose & face
1906	2	Undetermined tropical ulceration
1921	3	Malignant granuloma of nose
1921	4	Gangosa
1927	6	Noncommunicable gangrene of face
1929	7	Sarcolupus pernio
1931	9	Mutilating granuloma of nose & face
1931	12	Granuloma gangraenescens
1933	13	Progressive lethal granulomatous ulceration of nose
1933	15	Rheumatoid granulomatosis
1935	19	Atypical lymphosarcoma
1938	25	Gangrenous osteomyelitis of paranasal sinuses
1939	26, 27	Peculiar rhinogenous granuloma involving arterial system & kidneys
1940	28	Massive destruction of face
1941	29	Granulomatous ulcer of unknown etiology
1942	30	Chronic infectious granuloma of nose
1942	31	Hyperallergic Boeck's disease
1944	35	Chronic granuloma associated with polyarteritis nodosa
1945	36	Osteomyelitis necroticans faciei
1946	37	Periarteritis nodosa in granuloma of unknown etiology
1948	40	Wegener's granulomatosis
1949	42	Lethal granulomatous ulceration involving the midline facial tissues
1949	43	Nonspecific incurable ulcer on basis of anaphylactic reaction
1950	44	Giant cell granuloma with lesions resembling periarteritis nodosa
1950	49	Malignant mesenchymoma of nasomaxillary region
1953	55	Respiratorenal polyarteritis nodosa
1956	69	Granuloma of nose & necrotizing arteriolitis

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TABLE 2.—*Clinical Findings in 124 Cases of (Lethal Midline Granuloma—*

Case & Ref.	Age	Race & Sex	Early Symptoms	Duration of Disease: Prodromal Stage	Duration of Disease: Active Stage	Respiratory Tract: Upper Respiratory Tract	Respiratory Tract: Larynx, Trachea, & Pulmonary
1 (1)	28	WM	Persistent nasal discharge	?	9 mo.	Destruction & slough of entire nose, palate	--
2 (2)	44	NM	Purulent nasal discharge with obstruction	6 mo.	18 mo. +	Saddle nose; alae destruction; pharynx ulcers	Granuloma in larynx
3 (3)	68	WM	Blocked nose; loss of taste & smell; purulent nasal discharge	8 yr.	4½ yr.	Saddle nose; destruction of septum, turbinates, hard palate; otitis media	--
4 (3)	67	WM	Discomfort in nose 4 wk.	? wk.	1 yr. +	Destruction of septum, palate, maxillae	?
5 (4)	38	WM	Foul nasal discharge; lump inside nose	?	17 mo.	Diffuse nasal destruction; mouth & nose 1 cavity	?
6 (5)	42	WM	Nasal obstruction, persistent	?	8 yr.	Destruction of septum, palate, maxillae	Bronchopneumonia
7 (6)	26	WF	Purulent nasal discharge	?	16 mo.	Destruction of bone, cartilage, & skin of nose	Circumscribed pulmonary nodules, pleuritis
8 (7)	29	WM	Nasal catarrh; crusting; epistaxis	2 yr.	1 yr.	Destruction of nose, palate, maxillae, upper lip	--
9 (8)	60	WM	Nasal discharge	?	7 mo. +	Destruction of nose & palate; nose & mouth 1 cavity	--
10 (8)	30	WM	History of "atrophic rhinitis"	?	23 mo.	Destruction of nose, sinuses, palate; nose & mouth 1 cavity	Laryngeal granuloma
11 (8)	33	WM	Sudden onset of frequent epistaxes	?	5½ mo.	Nose & palate destruction	Laryngeal granuloma
12 (9)	32	WF	Nasal obstruction; fetid nasal discharge	6 mo.	12 mo.	Destruction of nose, palate, maxillae; mouth & nose 1 chamber	--
13 (10)	71	WM	Maxillary sinusitis	6 mo.	6 mo.	Destruction of bones of nose & all sinuses	Tracheal granulomas, pneumonia
14 (11)	50	WM	Headache; fetid, purulent nasal discharge after "endonasal operation" for ?	?	16 mo.	Diffuse destruction & facial bones	Tracheal & pulmonary granulomas
15 (12)	62	WF	Nasal swelling, obstruction	?	18 mo.	Destruction with gangrene of nose, palate, upper lip, sinuses	?
16 (13)	31	WM	Unilateral nasal obstruction; purulent discharge	3 mo.	10 mo.	Gradual destruction of contents of nasal cavity, maxillae, palate	Granuloma of larynx
17 (13)	36	WM	Nasal stuffiness	2 yr.	10 mo.	Destruction of septum, turbinate, maxillary bone, palate perforation, otitis media	--
18 (13)	39	WM	Pain over maxillary antrum	2 yr.	16 mo.	Destruction of maxillary antrum, cheek, palate	Pneumonitis
19 (13)	37	WM	Unilateral, painless nasal swelling	3 mo.	8 mo.	Destruction of septum, lateral wall of nose	Laryngeal granuloma
20 (14)	?	WM	Swollen spot on hard palate; purulent nasal discharge	?	1 mo.	Destruction of septum; palate perforation	?

Fatal Granulomatosis of the Respiratory Tract (Wegener's Granulomatosis)

Other Clinical Manifestations of Systemic Disease					
Renal, NPN, Albumin, Alb. Sediment	Joints	Skin (Diffuse)	Other	Histologic Exam.	Remarks
--	--	--	Ocular	Autopsy	Clinical diagnosis: III syphilis, mycosis fungoides, sarcoma
--	?	?	?	Biopsy only	Fate unknown; destructive process started after operation (nasal polypectomy)
--	--	--	Ocular	Restricted autopsy	Clinical diagnosis: malignant granuloma
?	?	?	Peripheral neuritis	Biopsy only	"Cure" by radium
?	?	?	?	Biopsy only	Outside death; clinical diagnosis: "gangosa," a tropical disease; patient never visited tropics
--	--	+	Ocular	Biopsy only	Destructive process started after submucous resection; radium therapy no help; fatal ending
--	--	+	--	Autopsy	Clinical diagnosis: "noma"; x-ray therapy no help
--	--	+	Ocular	Autopsy	Clinical diagnosis: "lupus pernio or lupus asphyxia"
?	?	+	?	Biopsy only	Fate unknown; pathologic diagnosis; "lymphogranulomatosis"
?	?	--	Ocular	Biopsy only	Death due to cachexia
?	?	?	?	Biopsy only	Death due to cachexia
?	?	?	Ocular	Biopsy only	Diagnoses prior to death: ? III syphilis, mycosis fungoides, sarcoma
+	--	--	Ocular C.N.S.	Autopsy	Destructive process started after "operation for relief of sinusitis"
+	+	+	Ocular	Autopsy	Stormy, downhill course after Caldwell-Luc & maxillectomy surgery; cause of death: "cachexia & weakness"
+	?	+	Ocular	Autopsy	X-ray therapy made patient worse; death due to vascular failure; diagnosis: osteitis necroticans faciei
--	--	--	--	Autopsy	Clinical diagnosis: gumma of nose; negative serologic test; x-ray therapy without help
--	--	+	--	Biopsy only	Destructive process started after submucous resection & tooth extraction; x-ray therapy without help; death after severe epistaxis requiring carotid ligation
--	--	--	--	Biopsy only	Destructive process started after maxillary antrum operation; death due to pneumonia
--	--	+	Ocular	Autopsy	Terminal septicemia with leukopenia
?	?	?	Ocular	Biopsy only	Stormy, downhill course with slough of entire middle of face after external ethmoid operation; death

TABLE 2.—Continued

21 (15)	44	WM	Upper respiratory infection with eyelid suppuration	?	?	Bone destruction of maxillary sinus & mastoid; pan sinusitis	Laryngeal & tracheal granuloma
22 (16)	30	WF	Purulent nasal discharge	16 mo.	20 mo.	Bone necrosis of septum, lateral nasal walls, palate; alar slough; tonsil granulomata	Pulmonary radiodensities
23 (17)	31	WM	Frontal headache; orbital pain; purulent nasal discharge	2 mo.	2 mo.	Destruction of lateral nasal wall, septum, maxilla, frontal & ethmoid sinuses	--
24 (18)	24	WF	Nasal obstruction	?	?	Osteomyelitis of hard palate	Ulceronecrotic laryngitis
25 (19)	47	WM	Painful nose & upper teeth	1 mo.	6 mo.	Gangrenous ulceration of nasopharynx, oral pharynx; palate perforation; antral sinusitis	?
26 (20)	54	WM	Frontal sinusitis; purulent nasal discharge	?	30 mo.	Progressive sequestration of nasal bones, ethmoids, orbits	?
27 (20)	26	WM	Fetid nasal discharge	?	9 mo.	External nose sloughed away; ethmoid & orbital bone destruction	?
28 (21)	50	WM	Nasal polyps; nasal discharge with crusts	6 mo.	3 mo.	Destruction of lateral nasal walls, maxillary alveolar ridges	?
29 (21)	54	WM	Persistent purulent nasal discharge after electrocoagulation of furuncle in nasal vestibule	4 mo.	6 mo.	Destruction of septum, lateral nasal wall	?
30 (22)	37	WM	Traumatic ulcer, upper lip	6 mo.	5 mo.	Slough of nose, maxillae, & teeth, both lips	?
31 (23)	53	WM (Persian)	Nasal discharge; pain; swelling at medial canthus of eye	?	8 mo.	Pansinusitis; bone sequestra from nose, ethmoids	Productive purulent cough; patchy pneumonitis
32 (24)	50	WM	Epistaxis; purulent nasal discharge	?	3 yr.	Bone sequestra from nose; slough of skin & bone of maxillary antrum	?
33 (24)	45	WF	Ulcerating infection inside nose	?	3 yr.	Granulomatous ulcer of nasal septum & palate; bone sequestra	?
34 (25)	12	WF	Nasal discharge & swelling of cheek following scarlet fever	4 mo.	6 mo.	Granuloma of nose; necrosis of maxillary bone; sinusitis; palate & septum destroyed	Pneumonia & atelectasis
35 (26, 27)	38	WM	Coryza; nasal obstruction; maxillary sinus pain	2 mo.	4 mo.	Saddle nose; otitis media; sinusitis; septal perforation; necrotic stomatitis	Laryngeal granuloma; pulmonary infiltrates
36 (26, 27)	36	WF	Nasal obstruction; discharge	3 mo.	4 mo.	Destruction of septum, turbinates; sinusitis; otitis media	Bronchopneumonia; laryngeal granuloma
37 (26, 27)	33	WF	Headache; bloody fetid purulent nasal discharge	?	4 mo.	Granuloma of nasal cavity; sinusitis	Laryngeal granuloma with respiratory obstruction
38 (28)	38	WM	Discharge from nose	4 mo.	12 mo.	Ethmoid & maxillary sinusitis; necrosis of bones of nose & sinuses	Bronchopneumonia
39 (29)	51	WM	Nasal stuffiness; mucoid nasal discharge; headache	5 mo.	6 mo.	Destruction of bones of nose	--

TABLE 2.—Continued

+	+	--	Eosinophilia, ocular	Autopsy	Active stages severely exacerbated by enucleation, antrotomy, & mastoidectomy; eosinophilia after antrotomy
?	?	+	Ocular; hepatosplenomegaly	Autopsy	X-ray therapy without help; terminal cachexia
--	--	--	C.N.S.	Autopsy	Destructive process started after ethmoidectomy
+	--	+	Splenomegaly	Autopsy	Terminal uremia; histological diagnosis by Aschoff; "malignant granuloma"
?	?	?	?	Biopsy only	Destructive process started after multiple tooth extractions (maxillary) & nasopharyngeal biopsy; death due to hemorrhage of large artery at superior pole of tonsil
?	?	?	Ocular	Biopsy only	Active disease started after frontal sinus operation; death due to "septicemia"
?	?	?	Ocular	Biopsy only	X-ray therapy without help; death due to hemorrhage in spite of carotid ligation
?	?	?	Ocular	Biopsy only	Death due to severe epistaxis
?	?	?	Ocular	Biopsy only	Destructive process started after "radical mastoid antrum operation"; terminal septicemia
?	?	?	Splenomegaly	Autopsy restricted	False-positive serologic test for syphilis; death due to hemorrhage & cachexia
?	?	+	C.N.S.; ocular splenomegaly	Autopsy	X-ray therapy without help; destructive process started after radical debridement of nose & ethmoids; death due to meningitis & cachexia
?	?	?	?	Biopsy only	Death due to hemorrhage from erosion of internal maxillary artery
?	?	?	?	Autopsy	Clinical diagnosis; gangrene of nose
?	?	?	Hydropericardium	Autopsy	Destructive process started after antral window & exacerbated after Caldwell-Luc; death due to hemorrhage; while in bed patient grew to 180 cm. (nearly 6 ft.)
+	+	+	+	Autopsy	Clinical diagnosis: "bizarre respiratory infection"; death due to uremia
--	+	--	Heart (ECG changes); Eos. 5%	Autopsy	Clinical diagnosis: gumma; negative serologic test for syphilis; destructive process exacerbated by biopsy of nose
+	--	+	WBC 2,800; Eos. 15%-20%	Autopsy	No evidence of bone involvement
--	--	--	Ocular; C.N.S.	Autopsy	Destructive process started after frontal-ethmoid exploration & antrotomy (author's opinion: destruction of face due to anergic state)
--	+	--	--	Biopsy only	Destructive process started after Caldwell-Luc, ethmoid biopsy, turbinate cauterization; death due to massive nasal hemorrhage

TABLE 2.—*Clinical Findings in 124 Cases of Fatal (Lethal Midline Granuloma—*

Case & Ref.	Age	Race & Sex	Early Symptoms	Duration of Disease		Respiratory Tract	
				Prodromal Stage	Active Stage	Upper Respiratory Tract	Larynx, Trachea, & Pulmonary
40 (29)	35	WM	Thin foul nasal discharge	7 mo.	4 mo.	Destruction of septum; pansinusitis	--
41 (29)	57	WM	Nasal stuffiness, discharge	5 mo.	7 mo.	Granuloma of nose; involvement of turbinate	Advanced silicosis
42 (30)	22	WF	Nasal discharge; ulcer in nose, facial pain & swelling	6 yr.	5 mo. +	Destruction of facial bones; slough of nasal tip; frequent hemorrhages	?
43 (31)	20	WF	Tonsillitis; pharyngeal pain; odynophagia; rhinitis	1 yr.	3 yr.	Diffuse granuloma of nose, pharynx, & tonsils	Laryngeal granuloma; diffuse spotty shadows in both lungs
44 (32)	62	WM	Nasal obstruction, discharge	5 yr.	2½ yr. +	Destruction of bones of nose; palate perforation	--
45 (33, 34)	44	WF	Nasal obstruction; sinus infections	?	30 mo.	Destruction of facial bones	--
46 (33, 34)	30	WM	"Ozena for 16 yr."	16 yr.	21 mo. +	Necrosis of bones of septum, ethmoids; nasal alar destruction	--
47 (35)	67	WF	Nasal crusting; epistaxis; "atrophic rhinitis"	?	13 mo.	Saddle nose	Productive cough; dense hilar shadows; interstitial fibrosis
48 (36)	24	WF	Discharge from nose "some length of time"	?	2 mo.	Gangrenous osteomyelitis of nose & sinuses	Patchy pneumonitis
49 (36)	41	WM	Blister of hard palate; nasal crusting; facial pain	3 mo.	6 mo.	Gangrenous osteomyelitis of nose, sinuses, facial bones	Pneumonitis
50 (37)	38	WM	Sinus trouble; later bronchiectasis	10 yr.	2 mo.	Ulceration of nose & tongue	X-ray picture of bronchiectasis
51 (38)	58	WM	Trigeminal neuralgia; carious teeth; nasal discharge	?	5 mo.	Destruction of maxillae; turbinates	Pneumonia
52 (39)	34	WF	Gingival ulcer after tooth extraction (upper) which did not heal	?	8 mo.	Pansinusitis; no bone destruction	Pulmonary infiltrates on x-ray
53 (39)	62	WF	Cough; purulent sputum, recent duration	?	3 mo.	--	Pulmonary consolidations & bronchiectasis on x-ray
54 (40)	57	WF	Nasal inflammation; earache with difficulty in hearing	?	3 mo.	Scanty data	Rounded parenchymal densities in lungs on x-ray
55 (41)	39	WM	Sinusitis; nasal stuffiness; mucoid secretions	7 yr.	10 mo.	Widespread nasal, facial & palatal bone destruction	Pneumonia
56 (41)	27	WM	Nasal obstruction; pain in nose & teeth	2 mo.	4 mo.	Bones of nose, palate, maxillae necrotic	Nodular densities in lungs
57 (42)	48	WF	Recurrent mouth ulcers; purulent nasal discharge	2 yr.	21 mo.	Granulomatous ulcers of nose, palate, pharynx; sinusitis	Hoarseness; pleuritic pains
58 (42)	45	WM	Sinusitis for years; swollen lymph nodes in neck	?	20 mo.	Granulomatous involvement of soft tissue & bone destruction in nasal cavity & sinuses	Pleural fluid

Granulomatosis of the Respiratory Tract—Continued
Wegener's Granulomatosis)

Other Clinical Manifestations of Systemic Disease					
Renal, NPN, Albumin, Alb. Sediment	Joints	Skin (Diffuse)	Other	Histologic Exam.	Remarks
?	?	?	Ocular	Biopsy only	Death due to "sepsis"
?	?	?	Intestinal obstruction	Biopsy only	X-ray therapy without help; active disease exacerbated after turbinectomy; no diagnosis at death
?	?	?	?	Biopsy only	X-ray therapy without help; active disease with bone destruction after trauma; author felt "fatal determination inevitable"
+	+	+	Ocular C.N.S.; Eos. 8%	Autopsy	Terminal "coma"; author calls disease "hyperallergic Boeck's
+	--	--	--	Biopsy	X-ray therapy with temporary remission; destructive process exacerbated after nasal debridement operation; no further follow-up
?	?	?	?	Autopsy	X-ray therapy without help; terminal cachexia; active & destructive disease started after ethmoid & maxillary sinus operation
--	--	--	Eos. 4%	Biopsy only	Eczema in childhood; "cure" by x-ray therapy
+	--	--	Parotitis	Autopsy	Terminal uremia; author's diagnosis: "chronic granuloma, associated with periarteritis nodosa"
--	--	--	--	Autopsy	Active disease started after frequent antral punctures; violent gangrenous bone destruction after maxillary antrum "operation"
--	--	--	--	Autopsy	Author calls this "noma"
+	--	+	--	Autopsy	Ulcerating granulomatous process with downhill course started after lobectomy for bronchiectasis
?	?	?	?	Autopsy	Final diagnosis: "unidentified infection or unusual type of sarcomatous change"
+	--	--	5% Eos.	Autopsy	Clinical diagnosis: "Addison's disease with cachexia and exhaustion"
+	--	--	--	Autopsy	Clinical diagnosis: "pulmonary tumor, metastatic to kidney"; terminal uremia
?	?	?	?	Autopsy	Clinical diagnosis: "kidney tumor with pulmonary metastases"; upper respiratory tract not examined at autopsy
--	--	--	Ocular; C.N.S.	Autopsy	Destructive process, violent, after trephine of frontal sinus, ethmoidectomy, Caldwell-Luc operations; terminal cachexia
--	--	+	--	Autopsy	X-ray therapy without help; cachexia due to pneumonia & cardiac insufficiency
--	--	+	Ocular	Autopsy	X-ray therapy without improvement; nasal operation without exacerbation; death due to "exhaustion"
--	--	--	Ocular; WBC 68,000; 90% lymph.; later normal	Autopsy	X-ray therapy with temporary help; bilateral antral windows with temporary improvement, then destructive process with onset of U.R.I.s

TABLE 2.—Continued

59 (42)	21	WM (Mexican)	Pain in face, sanguinopurulent discharge after "sinus canalization"	7 mo. +	2 mo.	Destruction of septum; granuloma of nose, sinuses, & palate	Pneumonitis
60 (43)	36	WM	Nasal pain & pressure	?	?	Destruction of bones of nose, septum, maxilla; sinusitis	Bronchopneumonia
61 (43)	49	WM	Sinusitis & nasal discharge	10 mo.	18 mo.	Destruction of bones of nose, septum, maxillae, palate, ethmoids, frontal sinuses	Bronchopneumonia
62 (44)	23	WM	Nasal obstruction & discharge	2 mo.	4 mo.	Septal perforation; granuloma of nose; sinusitis	Edema of larynx
63 (45)	48	WM	Alveolar ulcer; nasal discharge; oral antral fistula	16 mo.	7 yr. +	Destruction of bone about maxillary antrum & orbit	Spontaneous pneumothorax
64 (46, 47)	34	WF	Nasal obstruction; epistaxis after tonsillectomy; local anesthesia	?	3 yr.	Necrosis of septum & turbinates	?
65 (46, 47)	58	WM	Nasal obstruction since childhood due to injury; nasal swelling after S.M.R.	?	2 yr.	Granuloma of nose, soft palate	Granulomatous ulceration of false cords; hoarseness
66 (46, 47)	32	WF	Epistaxis, dysphagia	?	7 mo.	Granuloma of nose, pharynx; palate perforated with bone necrosis	Granuloma of larynx
67 (46, 47)	34	WM	Nasal discharge; medial canthal swelling	?	2½ yr.	Polypoid granuloma in nose; necrotic bone in antrum & ethmoid, frontal sinuses	Pulmonary edema
68 (46, 47)	28	WM	Tonsillitis; purulent nasal discharge	?	18 mo. +	Necrosis of nasal bones, palate; canthal perforation	?
69 (46, 47)	42	WM	Swelling of nose & cheek	?	6 mo. +	Necrosis of bones of nose with sequestra; sinusitis	?
70 (46, 47)	49	WF	Infection of lacrimal sac; nasal ocular angle swelling	?	8 mo.	Necrosis of bones of nose, antrum, ethmoids, orbit	?
71 (46, 47)	27	WM	Nasal swelling & discharge after fracture sustained in boxing	?	10 mo. +	Hard palate & turbinate necrosis; after sinus operation	?
72 (48)	52	WF	Pain in face & eye	2 mo.	3 mo.	Granulomatous sinusitis; necrosis of bone in nasal cavity	Pulmonary circumscribed density
73 (48)	52	WM	Allergic polyps removed; nasal obstruction	5 yr., 4 mo.	8 mo.	Osteitis of frontal sinuses, rubbery granuloma in nose; otitis media; erosion of septum	?
74 (49)	51	WM	Swelling of nasal ala after sinusitis; history of atrophic rhinitis	?	16 mo.	Necrosis of bones of nose, palate, maxilla; mouth & nose single cavity	--
75 (50)	69	NF	Weakness; productive cough; anorexia; weight loss	2 mo.	3 mo.	No ENT exam.	Densities in both lung fields on x-ray
76 (51)	31	WM	Alternate nasal obstruction	2 yr.	5 mo.	Granulomatous ulceration of nose & nasal pharynx	Laryngeal granuloma; terminal pneumonia
77 (51)	17	WF	Chronic nasal obstruction; nasal crusting; epistaxis since scarlet fever, age 5	10 yr.	2 yr.	Granulomatous ulcer of nose, nasal pharynx; palate necrosis; sinusitis	Laryngeal granuloma

TABLE 2.—Continued

+	+	+	Heart, ECG changes	Autopsy	Active disease appeared to start after canalization of antrum; exacerbation & diffuse organ involvement after antral-nasal exploration, with rapid downhill course
--	--	--	--	Autopsy	X-ray therapy without help; death due to sepsis & bronchopneumonia
--	--	--	Ocular	Autopsy	Destructive process started after Caldwell-Luc operation & exacerbated by 3 subsequent sinus operations
+	--	--	Ocular	Autopsy	Rapid downhill course after Caldwell-Luc operation; terminal oliguria
--	--	--	Ocular	Biopsy only	Destructive process exacerbated by Caldwell-Luc & exenteration of destroyed facial bones; remission on cortisone (Compound E); fate not known
?	?	?	?	Biopsy only	X-ray therapy no help; active disease started after tonsillectomy; bone destruction started after Caldwell-Luc & exacerbated after radical frontal sinus operation; terminal cachexia
?	?	+	Ocular	Biopsy only	X-ray therapy no help; active disease started after S.M.R.; death
?	?	?	?	Biopsy only	X-ray therapy no help; death due to hemorrhage & cachexia
?	?	?	Ocular	Biopsy only	X-ray therapy; destructive process started after Caldwell-Luc & exacerbated after ethmoidectomy; death due to cachexia & pulmonary edema
?	?	?	Ocular	Biopsy only	X-ray therapy with "healing"; plastic operation to canthal area; considered possible "cure"; fate not known
?	?	?	Ocular	Biopsy only	X-ray therapy with 6-year follow-up; considered "cure by x-ray"
?	?	?	Ocular	Biopsy only	X-ray therapy without help; destructive process exacerbated after "sinus" operation; death with massive facial deformity
?	?	?	?	Biopsy only	Destructive process started after "Denker operation"; x-ray therapy with remission; fate not known
+	--	--	Ocular	Autopsy	Active & destructive disease started after "radical antrotomy"; death due to uremia & cachexia
+	--	--	--	Autopsy	Destructive process started after frontal sinus operation with rapid downhill course; diffuse respiratory & visceral organ involvement at autopsy
--	--	--	--	Biopsy only	Death due to cachexia; no lymph nodes in head & neck
+	--	--	--	Autopsy	Rapid downhill process which involved lower respiratory tract, kidneys, & spleen; terminal renal failure
+	--	+	Eos. 4%	Autopsy	X-ray therapy without help; serologic test for syphilis, false positive
--	--	--	--	Autopsy	Terminal hyperpyrexia & exhaustion; mechlorethamine hydrochloride (nitrogen mustard) therapy without help; x-ray therapy without help

TABLE 2.—*Clinical Findings in 124 Cases of Fatal (Lethal Midline Granuloma—*

Case & Ref.	Age	Race & Sex	Early Symptoms	Duration of Disease: Prodromal Stage	Duration of Disease: Active Stage	Respiratory Tract: Upper Respiratory Tract	Respiratory Tract: Larynx, Trachea, & Pulmonary
78 (51)	53	WM	Chronic nasal obstruction, with crusting since gastric tube in place for several days	8 yr.	1 yr. +	Necrosis of bones of lateral nasal wall	--
79 (52)	50	WF	Nasal obstruction; crusting; purulent discharge; epistaxis	1 mo.	14 mo. +	Saddle nose; destruction of septum	Ulcerating glanuloma of larynx
80 (53)	43	WM	Headache; epistaxis	?	6 mo.	Destruction of septum & lateral nasal wall; necrosis of temporal bone with otitis media	?
81 (54)	42	WM	Nasal obstruction; pain over frontal sinus; purulent nasal discharge	4 yr.	2 yr. +	Bone destruction of septum, turbinates; granulomatous pharyngitis	--
82 (55)	70	WM	Chills; fever; lung pain	?	2 mo.	--	Dense spots suggesting metastasis in both lung fields
83 (55)	41	WF	Sinusitis	2 mo.	12 mo.	Granulomatous sinusitis	Laryngeal granuloma; pulmonary nodular densities
84 (56)	31	WM	Nasal congestion; rhinorrhea; epistaxis	2 yr.	1 yr.	Granulomatous nasal mucosa; sinusitis	Diffuse nodular interstitial infiltration; laryngeal granuloma
85 (57)	60	WM	Nasal obstruction, discharge & swelling	?	7 mo. +	Destruction of nasal bones; granulomatous nasal mucosa	--
86 (58)	42	WM (Cuban)	Foul breath; nasal discharge	9 mo.	21 mo. +	Destruction of nasal bone, hard palate	--
87 (59)	40	WF	Severe sinusitis, associated with rib trauma; massive lung collapse	?	2 mo.	Red nasal mucosa, crusted with blood	Increased pulmonary density; granulomatous process on bronchial & lung biopsy
88 (59)	34	WM	Attacks of sinusitis	4 mo.	1 yr.	Epistaxis; nasal congestion; pansinusitis on x-ray (scanty data)	Normal chest x-ray
89 (59)	39	WM	Facial pain; thick nasal discharge	2 mo. +	3 mo.	Oral-antral fistula with maxillary bone destruction	Normal chest x-ray
90 (59)	39	WM	Sinusitis; otitis media	?	4 yr.	Saddle nose; pansinusitis; purulent	Ulcerative laryngitis; infiltrative densities in lungs
91 (59)	12	WF	Purulent rhinitis; sinusitis	1 mo.	2 mo.	Otitis media; granulomatous nasal mucosa	Multiple nodular shadows in lung fields
92 (59)	38	WM	Sinusitis; cough; low-grade fever	1 mo. +	3 yr. +	Severe destructive sinusitis with bone necrosis; saddle nose	Scattered nodular densities; granulomatous laryngitis
93 (60)	53	WF	Stuffy nose; serosanguinous foul nasal discharge	6 mo.	4 mo.	Necrosis of bones of nasal septum; granulomatous nasopharyngitis; sinusitis	--

Granulomatosis of the Respiratory Tract—Continued
Wegener's Granulomatosis)

Other Clinical Manifestations of Systemic Disease					
Renal, NPN, Albumin, Alb. Sediment	Joints	Skin (Diffuse)	Other	Histologic Exam.	Remarks
--	--	--	--	Biopsy only	Destructive process started after Caldwell-Luc operation; corticotropin (ACTH) therapy with improvement but without remission; no further follow-up
+	+	+	Eos. 10%	Biopsy only	Temporary remission with corticotropin and cortisone; fate unknown
?	?	?	4% Eos.	Biopsy only	Destructive process started after bilateral maxillary sinus operations; fulminating necrotic downhill process; death due to cachexia & hemorrhage
--	--	+	--	Biopsy only	X-ray therapy with temporary remission; 3-month follow-up
+	--	--	--	Autopsy	Terminal uremia; patient an example of lower respiratory tract & visceral involvement; usually very rapid downhill course
+	+	+	Ocular	Autopsy	Active stage started after sinus irrigation
+	--	+	18% Eos.	Autopsy	X-ray therapy without help; terminal uremia
--	--	--	Ocular	Biopsy only	Removal of necrotic bone & soft tissue by eyebrow incision; followed by corticotropin therapy; external lesion healed, but extension along floor of nose & septum; fate unknown
--	--	--	Ocular	Biopsy only	X-ray therapy, partial remission; no further follow-up
+	--	--	--	Autopsy	Rapid downhill course after incision & drainage of pulmonary granuloma; corticotropin therapy without help; terminal oliguria
+	+	+	Ocular	Autopsy	Downhill course after 2 operations on knee joint, involved with arthralgia; cortisone therapy without help; terminal uremia; many granulomas of lung at autopsy; no upper respiratory tract exam.
+	--	+	Ocular; peripheral neuritis	Autopsy	Terminal uremia; granulomas of lung at autopsy
+	+	--	14% Eos.	Autopsy	Rapid downhill course after mastoidectomy for suspected sigmoid sinus thrombosis
+	+	--	Seasonal hay fever	Autopsy	Death due to "accumulated blood and exudate in rhonchopulmonary passages"
+	--	--	Ocular	Biopsy only	Renal involvement after Caldwell-Luc operation; lobectomy without improvement; corticotropin & cortisone therapy with ineffective control of disease; mechlorethamine hydrochloride & x-ray therapy, TEM, testosterone, estrogens, snake venom without help; fate unknown
--	--	--	Ocular	Autopsy	Destructive process started after nasal polypectomy; corticotropin & cortisone therapy without help; disease confined to upper respiratory tract at necropsy

TABLE 2.—Continued

94 (60)	43	WF	Sinusitis; pain in face	1 mo. +	2 mo.	Granulomatous & destructive rhinitis & sinusitis, soft tissue & bone	-	--
95 (61)	59	WF	Ulcer, right nasal ala; nasal discharge	?	15 mo.	Destruction of bones of nose, palate; soft tissue necrosis		--
96 (62)	31	WM	Facial pain; sinusitis	?	2 mo.	Granuloma of septum; bone necrosis of lateral nasal wall		Density with cavitation in lung
97 (63)	28	WF	Nasal obstruction; purulent nasal discharge	2 yr.	5 yr. +	Destruction of septum, bones of lateral nasal wall, palate; sinusitis		--
98 (64-66)	57	WM	Nasal obstruction; fetid nasal discharge	2 yr.	2 mo.	Sinusitis; sequestra of bones from sinuses		--
99 (67)	?	WM	Pain in maxilla	?	2 yr.	Sequestra of bones of nose, palate, maxilla		--
100 (68)	43	WM	Severe nasal congestion; copious nasal discharge; fever	?	12 mo.	Destruction of cartilaginous septum; sinusitis		Granuloma of larynx
101 (69)	53	WM	Bilateral nasal obstruction; intermittent epistaxis	?	16 mo.	Granuloma fills nose		--
102 (70)	39	WM	Sinusitis & orbital cellulitis	?	26 mo.	Necrosis of bones of nose, sinuses, orbits, palate; otitis media		Bronchopneumonia
103 (70)	53	WM	Persistent nasal catarrh	?	16 mo. +	Pansinusitis; septal perforation		?
104 (70)	22	WF	Pansinusitis & nasal granuloma	?	9 mo. +	Destruction of lateral wall of nose & palate		?
105 (71)	24	WF	Nasal crusting; purulent discharge	?	5 mo. +	Nasal septum perforation; necrotic ulcers of tonsils & uvula; otitis media with mastoiditis		Granuloma of larynx; cavity in lung
106 (72, 73)	42	WF	Attack of pleurisy; anosmia	?	10 mo.	Granuloma of nose; septal perforation		Pleurisy, rounded nodular density in lung
107 (72, 73)	34	WF	Mild tonsillitis; arthralgia; deafness; nasal obstruction	?	6 mo.	Pansinusitis; ulcerated nasal mucosa; otitis media		Pneumonitis
108 (72,73)	33	WM	Otitis media; nasal stuffiness	?	9 wk.	Granuloma of nose, middle ear; pharynx ulcerated; sinusitis		Circular opacity in lung
109 (72, 73)	39	WM	Headache; swelling & soreness of gums; limb pain; nonproductive cough	?	7 wk.	Sinusitis; swelling of nose, alveolar ridge; ulceration of palate		Pulmonary consolidations
110 (74)	33	WF	Nasal obstruction; pink nasal discharge	1 mo.	9 mo.	Ulcerated granuloma of turbinates; septal perforation; sinusitis; otitis media		--

TABLE 2.—Continued

+	--	+	Ocular	Autopsy	Active disease started after tooth extraction; destructive process with downhill course after frontal sinus operation & thigh biopsy; granulomas of viscera on necropsy
?	?	--	Ocular	Biopsy only	X-ray therapy & semicarbazone without help; death due to cachexia & exhaustion; massive facial mutilation
+	+	--	Peripheral neuritis	Autopsy	Destructive process & generalized organ involvement after removal of nasal granuloma; cortisone no help; terminal renal failure
?	?	--	--	Biopsy only	"Right side of nose melted away" after Caldwell-Luc operation; x-ray therapy with apparent cure; plastic reconstruction of face, 1952
?	?	?	?	Biopsy only	Rapid downhill course after exenteration of "nasal, ethmoid, & maxillary cavities"; TEM & x-ray without help; patient died in "coma"
?	?	?	Ocular	Biopsy only	Active disease after tooth extraction (transmaxillonasal debridement) with rapid downhill course; patient in terminal state when discharged
--	--	+	Hepatomegaly	Autopsy	Destructive process started after removal of furuncle from nasal vestibule; subsequent biopsies made patient worse; x-ray therapy & prednisone (Meticorten) without help; allergic to penicillin & chloramphenicol (Chloromycetin); terminal periods of apnea; irrationality
+	+	+	Splenomegaly	Autopsy	X-ray therapy without help; terminal uremia
	+	--	Ocular	Autopsy	Active disease & destructive process started & exacerbated after consecutive ethmoidectomy, antrotomy, sphenoidectomy, excision of granuloma of orbit; cortisone produced temporary remission
?	?	?	Ocular	Biopsy only	Active disease & destructive process started after S.M.R. and nasal antrostomy; cortisone therapy; x-ray therapy with 8-mo. follow-up; "nose quiescent with foul crusts"
?	?	?	Ocular	Biopsy only	Destructive process started after Caldwell-Luc operation; x-ray therapy with remission, 5-mo. follow-up
+	+	+	Ocular	Autopsy	Death due to "otitis media with septicemia"
+	+	+	Peripheral neuritis	Autopsy	Lower respiratory tract involved first; upper respiratory lesions with destruction after thoracotomy; eosinophilia, systemic spread as well as antibiotic sensitivity after same operation; death due to peripheral circulatory collapse
+	+	+	--	Autopsy	Progression of nasal symptoms; terminal albuminuria
+	--	+	4% Eos.	Autopsy	Rapid downhill course with severe necrotizing angiitis at necropsy involving upper & lower respiratory tracts, as well as viscera
+	+	+	--	Autopsy	Terminal oliguria
+	--	+	Ocular; hepatosplenomegaly	Autopsy	Disease started in upper respiratory tract; destructive stage after excision of granuloma in cholecystectomy scar & skin of thigh; x-ray therapy & cortisone without help; terminal vascular collapse

TABLE 2.—*Clinical Findings in 124 Cases of Fatal (Lethal Midline Granuloma—*

Case & Ref.	Age	Race & Sex	Early Symptoms	Duration of Disease: Prodromal Stage	Duration of Disease: Active Stage	Respiratory Tract: Upper Respiratory Tract	Respiratory Tract: Larynx, Trachea, & Pulmonary
111 (75)	60	WM	Increasing nasal obstruction, malaise, weakness, & weight loss	15 yr.	2 yr.	Destruction of bones of nose, sinuses, & palate	?
112 (75)	34	WM	Inflamed nose with discharge	?	2 yr. +	Loss of nasal septum; palate perforation; maxilla & other facial bone destruction	?
113	27	WM	Bouts of flu; bloody nasal discharge; headaches	10 mo.	2 mo.	Destruction of bones of septum & sinuses	University of Michigan Multiple nodular densities; hemoptysis
114	49	WM	Bloody purulent nasal discharge; foul odor; crusting	5 yr.	16 mo.	Destruction of septum, turbinates; saddle nose; palate perforation; sinusitis	Negative chest x-ray
115	28	WF	Nasal obstruction; epistaxis; suppurative otitis media	16 yr.	3 yr., 2 mo.	Destruction of septum; sinusitis; saddle nose	Patchy pneumonitis
116	57	WF	Bloody purulent nasal discharge; hoarseness; fetid productive cough; cyanotic episodes	1 yr.	4 mo.	Destruction of septum	Laryngeal & tracheal granulomata
117	36	WM	Fetid purulent nasal discharge; facial pain	15 mo.	11 mo.	Slough of entire external nose; palate perforation	Pneumonia
118	38	WF	Fetid nasal discharge; suppurative otitis media	6 mo.	21 mo.	Destruction of septum, turbinates; palate ulcer	Granuloma of larynx & trachea
119	51	WM	Fetid nasal discharge	8 mo.	9 mo.	Slough of almost entire external nose	Negative chest x-ray
120	53	WM	Nasal crusting; purulent discharge	4 mo.	13 mo.	Granulomatous ulcers of septum, turbinates; bone denuded; sinusitis	Granuloma of larynx, trachea; pneumonitis
121	34	WM	Bloody purulent nasal discharge	1 mo.	3 yr., 7 mo.	Destruction of septum, turbinates; saddle nose; sinusitis	Pulmonary nodular density
122	50	WF	"Allergic rhinitis" 19 yr.	19 yr.	4 yr.	Destruction of septum, turbinates; saddle nose; suppurative otitis media	Laryngeal granuloma; multiple pulmonary nodular densities
123	52	WM	Persistent sore throat; tonsillitis	2 mo.	14 mo.	Destruction of septum; sinusitis; granuloma of tonsil	Granuloma of epiglottis; pneumonitis; lung abscess
124	52	WF	Nasal obstruction; crusting	5 yr.	12 yr.	Destruction of septum; ulcer of nasal ala	Negative chest x-ray

Granulomatosis of the Respiratory Tract—Continued
Wegener's Granulomatosis)

Other Clinical Manifestations of Systemic Disease					
Renal, NPN, Albumin, Alb. Sediment	Joints	Skin (Diffuse)	Other	Histologic Exam.	Remarks
?	?	?	Ocular	Biopsy only	S.M.R. of septum at time of active stage with bone destruction; exacerbation after debridement & sinus operation; x-ray therapy without help; terminal meningitis
?	?	?	Ocular	Biopsy only	Destructive process started after antrotomy & exacerbated after radical sinus & debridement operation; patient treated with cortisone but destruction continued; fate unknown
Hospital Cases					
--	--	--	C.N.S. with seizures	Biopsy only	Clinical diagnosis: infectious granuloma of brain, sinuses, and lungs
--	--	--	Blood loss anemia; splenomegaly	Biopsy only	Death elsewhere; no autopsy; x-ray therapy without help
--	+	+	Leukopenia; Eos.; ocular	Biopsy only	Death elsewhere; attributed to rheumatoid arthritis, coronary occlusion, nasal granuloma
+	--	--	--	Biopsy only	Death elsewhere; diagnosis: "glomerulonephritis, uremia"
+	--	--	Ocular	Autopsy elsewhere	Destructive process started after S.M.R.; virtually complete slough of nose, maxillae, & palate; x-ray therapy without help; autopsy gave no further information
+	+	+	Ocular; blood loss anemia	Biopsy only	S.M.R. in prodromal stage; ethmoidectomy in active stage, followed by renal & joint sequela; rapid downhill course; death due to overwhelming septicemia
--	--	+	Ocular; splenomegaly	Biopsy only	Death elsewhere
+	+	+	Blood loss anemia	Autopsy	Terminal granulomatous laryngotracheal obstruction; asphyxia
+	+	+	Ocular	Autopsy	Active stage followed nasal polypectomy; corticotropin and cortisone therapy without help; death due to "exhaustion"
--	+	+	Ocular	Autopsy	Active stage followed by extensive nasal polypectomy; corticotropin, cortisone and prednisone therapy with remission; death due to myocardial infarction, rupture, & tamponade
--	+	--	--	Biopsy only	Remission on cortical steroids; exacerbation with rapid downhill course after hip operation; death elsewhere
--	--	--	--	Biopsy only	Operation: removal of entire nasal septum & 3 turbinates; nasal plastic operation to release alar contracture; patient alive & well 10 yr. after operation

servations concerning the management of this bizarre disease, and to clarify the pathogenesis in the light of accumulated data.

Our observations are based upon 12 patients from the University of Michigan Medical Center afflicted with the disease and upon a review of the literature from 1897 to 1957—a period of 60 years in which approximately 176 cases were reported. We have selected 112 cases as those representative of this disease based upon certain criteria to be described.

Case Reports from the Medical Literature

The rhinopharyngological description of Stewart [13] and the rhinologic-systemic syndrome as described by Klinger [10] and Wegener [26,27] form the basis for the selection of cases described in this report. For the most part, the otolaryngologist has been inclined to restrict his interest to the condition as it involved the "midfacial tissues." Pathologists, dermatologists, and internists, attracted by the granulomatous lesions in systemic organs and the condition of the blood vessels, have in numerous instances paid little attention to the upper respiratory tract, both clinically and post mortem. Thus necropsy findings of the nose, paranasal sinuses, pharynx, and temporal bones are absent in several excellent publications, although the clinical picture and the biopsy specimens showed definite evidence of the disease.

Table 2 presents a summary of 124 cases, 112 from the medical literature (1897-1957) and 12 from University of Michigan Medical Center, that fulfill the clinical and pathological criteria. Several cases included by the authors listed in the first 75 references have been omitted because of duplication of case reports, atypical features, and insufficient published clinical and histological data to allow for adequate evaluation. This is also true of other cases [76-103] for similar reasons. However, enough common characteristics emerge to form a strikingly identifiable picture in spite of the variability in the histories of these selected patients.

Analysis of 124 Cases

Definition of the Disease Entity

Fatal granulomatosis of the respiratory tract is a febrile inflammatory illness, characterized by a progressively destructive granulomatous suppuration of the upper respiratory tract and adjacent tissues of the face and usually with manifestations of disseminated systemic necrotizing granulomatous angiitis. There may be laryngeal and bronchopulmonary granulomas. The outcome is invariably fatal and may be due to renal failure, overwhelming infection, inanition, uncontrollable hemorrhage, or peripheral vascular collapse.

Incidence and Distribution

The varied clinical interpretations and confusing anatomical diagnoses given to this disease over the past 60 years make it difficult to estimate the rate or range of occurrence. A statistical study (Table 3) would indicate that fatal granulomatosis of the respiratory tract is on the increase. However, this seemingly increased frequency may be attributed to greater awareness of the physician in recognizing the disease process. The previous emphasis on the local midfacial manifestations, coupled with the failure of recognition and correlation of systemic involvement have been major deterrents to accurate diagnosis and reporting.

A. Distribution According to Sex.—The distribution of 82 males to 42 females among the 124 cases represents a signifi-

TABLE 3.—*Reported Cases of Fatal Respiratory Tract Granulomatosis in Various Years*

Years	Cases, No.
1897-1919	2
1920-1929	9
1930-1939	27
1940-1949	36
1950-1957	50
Total	124

cant departure from the hypothesis of an equal frequency of the disease in the two sexes. The aberrant sex ratio cannot be attributed to the more frequent rejection of incompletely reported cases in females, since among the 39 cases of reported fatal granulomatosis (lethal midline granuloma —Wegener's granuloma) rejected, in 26 instances the person was a male. There appears, therefore, to be a significant difference in the attack rate between the two sexes. The difference between the two sexes (ratio of 2:1, M:F) is even more significant when one considers the rather late age of onset, since the proportion of males in the age group 40 through 59 in the population is smaller than the proportion of females. However, the data do not suggest a mechanism which would account for the difference in the incidence of the disease in the two sexes.

B. Distribution According to Age.—The average age at diagnosis (Table 2) of this disease in males is 42.9 years and in females 38.8 years. This difference is not statistically significant. Moreover, the average age of males among rejected cases, some of which probably represent true fatal granulomatosis, is 37.4 years; whereas among the females the average age was 40.3 years. Part of the apparent age difference may be an artifact.

The distribution of ages of males at diagnosis given in Figure 1 appears to be bimodal, with one peak occurring in the interval of 30-39 years (fourth decade of life) and the other at 50-59 years. However, the data do not depart significantly from a normal distribution with a mean of 42.9 years and a standard deviation of 11.7 years.

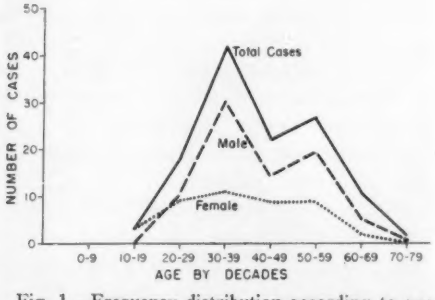

Fig. 1.—Frequency distribution according to age and sex of 124 cases of fatal hypersensitivity granulomatosis of the respiratory tract (lethal midline granuloma-Wegener's granulomatosis).

The distribution of ages of females at diagnosis (Fig. 1) is unimodal but appears somewhat platykurtic. However, the observed distribution again does not depart significantly from a normal distribution with a mean of 38.8 years and a standard deviation of 14.9 years.

C. Race and Geographic Distribution.—One of the most remarkable characteristics of this disease is its racial distribution; 122 out of 124 cases reported have occurred in patients of the white race, while only 2 patients were Negroes. Japanese investigators [86] have also reported cases, but these were sufficiently atypical and lacking in information to be excluded from this study. The ethnic groups include the Russian, Czech, Norwegian, Swedish, Italian, French, Mexican, Cuban, German, and British peoples, as well as various nationalities represented in the United States and Canada. The representati\ climate is temperate.

D. Occupation.—This case series is composed of patients from rural and urban areas, without specific orientation toward any occupation type. The metal and chemical worker is occasionally stricken but not with sufficient regularity to be statistically significant.

Clinical Features

There are two main forms of this disease—localized and generalized. The rhinopharyngological description of Stewart [13] comprises the localized form (lethal midline granuloma), and the rhinopharyngological-systemic syndrome described by Klinger [10] and Wegener [26,27] (Wegener's granulomatosis) is the generalized form. The symptomatology may be divided into two stages: premonitory, or prodromal, stage and the period of active disease—from which there is usually no return to

health. *The common denominator is onset of disease in the upper respiratory tract.* Occasionally lesions can be seen initially in the lower respiratory tract (larynx and pulmonary parenchyma), with subsequent participation of the upper respiratory structures, particularly the nose and paranasal sinuses (Table 2, Case 106). Occasionally the pulmonary parenchyma may be the only part of the respiratory tract involved (Cases 53 and 75).

A. Prodromal Stage.—The prodromal period may last from months to years (Table 2). At first the patient may be conscious of nasal stuffiness or obstruction. Then there is a persistent nasal discharge, serous or mucoid at the onset and sanguinopurulent later. The initial expression in some patients may be a blister or ulcer in the center of the hard palate or on the tonsils. The symptoms may be continuous or episodic, with evidence of healing, only to recur. As with disease in general, the individual patient varies in his tolerance of the effects of the disease. Sensitive highly strung people are more aware of minor disturbances and seek the physician's help early, while the rugged and phlegmatic may not be conscious of mischief until the disease is in its active stage. The early symptoms which have caused the patient to seek medical attention are enumerated in Table 4.

TABLE 4.—*Early Symptoms Which Caused Patients to Seek Medical Attention*

	Symptoms Referrable To	Cases, No.
(*a*)	Nose & sinuses	109
	Nasal obstruction	
	Epistaxis	
	Nasal discharge, persistent	
	Headache, frequent	
	Facial pain & swelling	
	Nasal furuncles, indolent	
	Nasal alar infections	
(*b*)	Lungs (initially)	3
	Cough	
	Hemoptysis	
	Pleuritic pain	
(*c*)	Pharynx & tonsils	4
	Odynophagia	
	Dysphagia	
	Persistent sore throat	
(*d*)	Larynx	2
	Persistent hoarseness	
	Airway obstruction	
(*e*)	Ears (in combination with (*a*))	6
	Sudden suppurative otitis media	
(*f*)	Palate (in combination with (*a*))	2
	Ulcer, blisters	
(*g*)	Alveolar ridge, gingiva, teeth	3
	Ulcers, loose teeth	

The physical findings in the prodromal stage usually raise no suspicion in the mind of the physician. Yellow-brown crust formation may be present in the nose, which upon removal shows superficial ulceration of the mucous membrane and which bleeds easily. A diagnosis of "atrophic rhinitis" may be made. Prescribed antiseptic instillations and irrigations give only temporary relief. "Indolent" furuncles in the nasal vestibule may appear and disappear. Mucopurulent discharge from the maxillary, ethmoid, and frontal sinuses with associated headache, pain, and swelling may be treated adequately with antibiotics only to recur.

B. Period of Active Disease.—Midfacial—Upper Respiratory Tract Area: Necrosis of integument, cartilage, or bone in the midfacial-nasal area usually heralds the period of active disease. With extensive septal cartilaginous and bony destruction a saddle nose deformity may appear (Fig. 2). The turbinates and nasal bones may also be destroyed (Fig. 3). Sometimes the skin of the nasomaxillary region is initially involved by the ulceronecrotic granulomatous process (Fig. 4). Occasionally the necrotizing lesion may begin in the center of the hard palate or in the pharynx (Case 123). If the maxillary alveolar processes are involved the teeth become loose and fall out. There is a progression of the mutilating gangrenous destruction to involve the maxillary and ethmoid sinuses and bones of the facial skeleton, with periodic elimination of sequestrae. Ocular involvement (Fig. 5) usually follows granulomatous sphenoiditis and may result in papillitis, chemosis, exophthalmos, and blindness.[104] Diffuse edema about the eyes, cheeks, and upper lip distort the features, and the necrosis may extend through the soft parts of the nose and face (Fig. 6). The final picture is that of loss of the midface. The deformity may be so

Fig. 2 (Case 121).—*A*, this photograph was taken 10 years prior to admission. *B*, the saddle-nose deformity appeared with extensive cartilaginous and bony destruction of the nasal septum.

Fig. 3 (Case 119).—The right nasal bone and nasal process of the maxillary bone have been destroyed. The skin surrounding this area was intensely erythematous with a central area of gangrenous perforation. The right middle turbinate and nasal septum also were destroyed.

Figure 3

Fig. 4 (Case 124).—There is a right nasal alar deformity as well as a saddle nose.

Figure 4

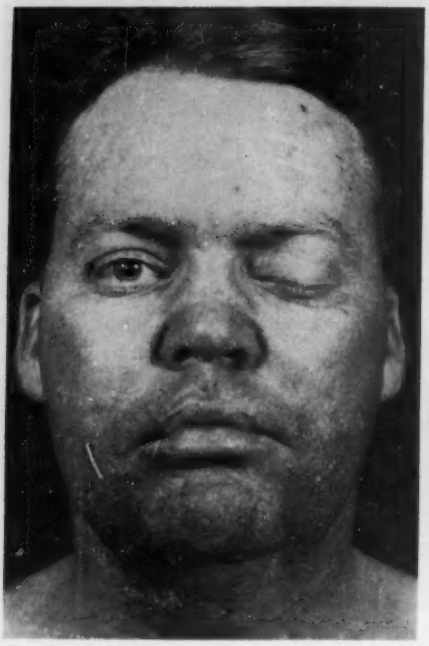

Fig. 5 (Case 121).—Involvement of the sphenoid sinuses herald the onset of ocular complications. There was paralysis of cranial nerves III and VI as well as amaurosis, O.S.

Fig. 7.—The final picture of fatal granulomatosis of the respiratory tract may be loss of the midface. The deformity may be so severe and shocking that the nose, mouth and pharynx are one cavity. Reproduced with permission from Dr. A. Touraine, Editor, *Annales de dermatologie et de syphiligraphie,* Paris, Masson & Cie.

Fig. 6 (Case 119).—In the terminal stage of fatal granulomatosis of the respiratory tract the diffuse edema about the eyes, cheeks, and upper lip distort the features. Gangrenous necrosis extends throughout the soft parts of the nose and face.

severe and shocking that the nose, mouth, and pharynx are one cavity (Fig. 7). The cervical chain of lymphatics usually are not palpable. Death may be due to overwhelming infection in spite of antibiotic therapy (Case 123), an exsanguinating hemorrhage from the nasomaxillary deformity (Case 39), or pharyngeal necrosis (Case 24) or inanition and generalized debility with complete exhaustion (Case 121 and Table 5).

TABLE 5.—*Clinical Status at Time of Death*

Condition	Cases, No.
Renal failure	25
Overwhelming infection	22
Cachexia and exhaustion	17
Exsanguinating hemorrhage	10
Laryngo-tracheal-bronchial obstruction	6
Peripheral vascular collapse	5
Pulmonary edema	1
Intestinal obstruction	1
Ruptured myocardium	1
Death not related to this disease (myocardial infarction)	1
Terminal clinical status not known	13
Total cases	102

TABLE 6.—*Sex and Age at Death—Systemic* Versus Nonsystemic Disease*

Age at Death	Males		Females		Total
	Systemic (Total)	Nonsystemic	Systemic (Total)	Nonsystemic	
10-19	0 (0)	0	2 (3)	1	3
20-29	3 (6)	3	3 (4)	1	10
30-39	19 (23)	4	9 (11)	2	34
40-49	5 (11)	6	7 (8)	1	19
50-59	9 (18)	9	5 (6)	1	24
60-69	1 (2)	1	4 (5)	1	7
70-79	2 (3)	1	0 (0)	0	3
Not known	2 (2)	0	0 (0)	0	2
Total	41 (65)	24	30 (37)	7	102

* Organ manifestations other than respiratory tract.

The Lower Respiratory Tract: Ulceronecrotic granulomatous lesions are frequently seen in the larynx and trachea. Airway obstruction as a result of suppuration, hemorrhage, and accumulated necrotic tissue can occasionally cause the death of the patient (Case 120). Attention may be directed to the lungs because of hemoptysis, chronic cough, or unresolving pneumonia. A chest x-ray frequently reveals nonspecific parenchymal infiltrations or nodular densities with excavation which suggest neoplasm or tuberculosis. Any part of the lung may be involved.

Systemic Manifestations: *The lesions of fatal respiratory tract granulomatosis are not limited only to some part of the respiratory tract. The patient may have symptoms referable to other organs.* Transient episodes of arthritis (Case 121), neuritis (Case 96), carditis (Case 59), acute splenic tumor (Case 24), and widespread granulomatous and/or hemorrhagic lesions of the skin (Case 122) have been seen. At times when the patient appears in a remission signs of renal damage appear (Case 121), often heralded by microscopic hematuria, albuminuria, and cylinduria. There may be a sudden gross hematuria and oliguria with death in uremia (Case 109). Often renal insufficiency is associated with roentgenographically observed pulmonary damage; features consistent with a vascular-granulomatous disease.

C. The Problem of Systemic Disease.—It is obvious that when distant organ involvement is seen ante mortem and post mortem, the person has a generalized disease (Table 6). The distribution of systemic disease by sex and autopsy does not appear to be the effect of sex, since it appears that virtually every autopsied case has systemic involvement (Table 7). *Systemic involvement is the rule rather than the exception,* although in a substantial proportion of cases the demonstration of systemic involvement is an autopsy finding. For the cases in the literature where no systemic involvement is described, one has therefore to be cautious in interpretation.

TABLE 7.—*Frequency of Systemic* Involvement by Sex and Occurrence of Autopsy*

	Male		Female		Total
	Autopsy	No Autopsy	Autopsy	No Autopsy	
Systemic	35	6	27	3	71
Nonsystemic	4	20	2	5	31
Total	39	26	29	8	102

* Organ manifestations other than respiratory tract.

TABLE 8.—*Death and Survival Data for Total Cases Reported*

Fate	Cases, No.
(*a*) Known deaths	102
(*b*) Fate not known at report	7
(*c*) Survival	
By surgery	1 (Case 124)
By x-ray therapy	4 (Cases 46, 68, 69, 97)
By radium therapy	1 (Case 4)
(*d*) Remissions (by steroid & x-ray therapy) but final outcome not known	9
Total	124

It would appear that the clinical statement of nonsystemic disease would be found to be incorrect in many instances if adequate examinations were made.

Survival

Of the total 124 cases herein reported there are 102 known deaths (Table 8). The disease appears to affect males and females of all ages, but most frequently in the fourth and fifth decades of life. It seems to appear in persons of good previous health, generally without histories of atopic allergy, asthma, or other hypersensitivity. It appears by *age at diagnosis* (Fig. 1), as well as by *age at death* (Table 6), that survival is only a matter of months for most patients in the active phase of this disease.

Roentgenographic Features of Fatal Granulomatosis of the Respiratory Tract

The roentgen findings in the prodromal stage or in the early period of active disease parallel the clinical manifestations. When the disease is unilateral in origin and granulomatous lesions can be seen in the nose clinically, there invariably is roentgen evidence of paranasal sinus inflammation. Maxillary sinus involvement is usually the most frequent and the first to be detected by x-ray, whether by primary extension or by ostium obstruction from granulation tissue in the nose (Table 9). This is the pattern in all the University Hospital cases and in all those of the reviewed literature [1-75] where roentgenograms were reported. As the lesion progresses all the cases will have bilateral maxillary sinus disease. An air-fluid level as seen in acute sinusitis has not been encountered in these cases. Clouding and thickening of the mucous membrane of the maxillary sinus is usually the roentgen finding in the early stages and is nonspecific (Fig. 8).

The ethmoid, frontal, and sphenoid sinuses may also be involved in the above order of frequency and usually to less degree than the maxillary sinuses (Table 10). It has been our experience that involvement of the sphenoid sinuses usually heralds orbital invasion, impaired vision, and impending blindness (Cases 121 and 122).[104] Although the roof of the sphenoid sinus may be eroded, the sella turcica has not been invaded in this group of cases.

Bone destruction can usually be seen roentgenographically, concomitant with perforation of the cartilaginous nasal septum. The earliest sites of destruction appear to be the perpendicular plate of the ethmoid, the vomer, and the inferior and middle turbinates. However, erosion of these bony components of the nasal septum may be difficult to detect by ordinary roentgenographic technique unless the bone structure is widely destroyed. The absence of the turbinate structures is readily noted on films, since they stand out in great contrast against the air-filled nasal cavity (Fig. 9). Evidence of such bone destruction was seen in 9 University Hospital cases (Table 9). As the destructive midfacial process continues, the thinning and eventual obliteration of the medial wall of the maxillary sinus will be noted on x-ray. The Caldwell projection is preferred to the Waters or Granger views, since the bones of the nasal chambers are seen in greater detail. The lateral projection is of value in recognizing sequestrated bone.

Some of the limitations of routine roentgenographic techniques of the paranasal sinuses can be overcome by tomography or laminography. Holvey [105] applied this tech-

TABLE 9.—*Roentgen Features of Fatal Granulomatosis of the Respiratory Tract*

	Paranasal Sinuses								
	Location, Sinuses				Bone Destruction			Pulmonary	
Case	Maxillary	Ethmoid	Frontal	Sphenoid	Nasal Septum	Inferior & Middle Turbinates	Medial Wall Maxillary Sinuses	Location	Type of Lesion
113	+	+	+	+	+	+	9	Bilateral	Multiple nodularities with cavitation
114	+	+	+	0	+	0	0	None	
115	+	+	0	0	0	0	0	Bilateral	Patchy pneumonitis
116	+	+	+	+	+	0	0	None	
117	+	0	0	0	0	0	0	None	
118	+	+	+	+	+	+	+	None	
119	+	+	+	+	+	+	+	None	
120	+	+	+	0	0	0	0	Bilateral	Patchy pneumonitis
121	+	+	+	+	+	+	+	Left lower lobe	Nodular mass
122	+	+	+	+	0	+	0	Bilateral	Multiple nodularities with cavitation
123	+	+	0	0	+	+	+	Left lower lobe	Pneumonitis with nodularity & cavitation
124	+	0	0	0	+	+	0	None	

Fig. 8 (Case 118).—Caldwell projection of paranasal sinuses shows unilateral involvement of the right frontal and maxillary sinuses, characterized by clouding and thickening of the mucous membrane. This is a roentgen finding in the early stage of active disease and is nonspecific.

Fig. 9 (Case 122).—Chronic pansinusitis with thickening of mucous membrane and clouding. The destruction of midfacial structures is well advanced with absence of turbinate structure. The nasal septum appears intact, although a perforation involving cartilage and bone is seen clinically. The nasal passages are filled with a homogeneous soft tissue density which represents granulomatous tissue clinically.

nique for appraising early bone destruction in the sinuses and nasal passages in cases of paranasal carcinoma. The patient is placed as for a Caldwell projection, and planes 4 to 7 cm. are filmed at 0.5 cm. levels. Comparison of tomograms of Case 121 with those of a normal person shows the midfacial destructive process which characterizes this disease (Fig. 10).

TABLE 10.—*Summary of Roentgen Manifestations in Twelve Cases of Fatal Granulomatosis of the Respiratory Tract*

	Cases	
	No.	%
I. Location (sinus)		
1. Maxillary	12	100
2. Ethmoid	10	71
3. Frontal	8	66
4. Sphenoid	6	50
5. Pansinuses	6	50
II. Appearance of lesion		
1. Thickening	12	100
2. Clouding	8	66
III. Bone destruction		
1. Nasal septum & turbinates	8	66
2. Medial wall	4	33
IV. Pulmonary lesions		
1. Patchy pneumonitis	2	16
2. Nodular	4	33
3. Cavitary	3	25
Total cases with pulmonary lesions	6	50

The roentgen appearance of the pulmonary lesions of fatal granulomatosis of the respiratory tract run almost the entire gamut of possible changes in pulmonary diseases and therefore are not diagnostic per se (Tables 9 and 10). Early, the widespread vasculitis of pulmonary vessels (seen histologically in this series and in cases reported in the literature[1-75]) is characterized roentgenographically by increased pulmonary vascular markings or as a soft interstitial pneumonitis. As the disease progresses, the appearance may change to a fleeting patchy bronchopneumonia or to a diffuse miliary nodularity. One of the most intriguing manifestations of this bizarre disease (described in the literature and present in three cases of this series) is the development of asymptomatic and clinically unrecognizable circumscribed nod-

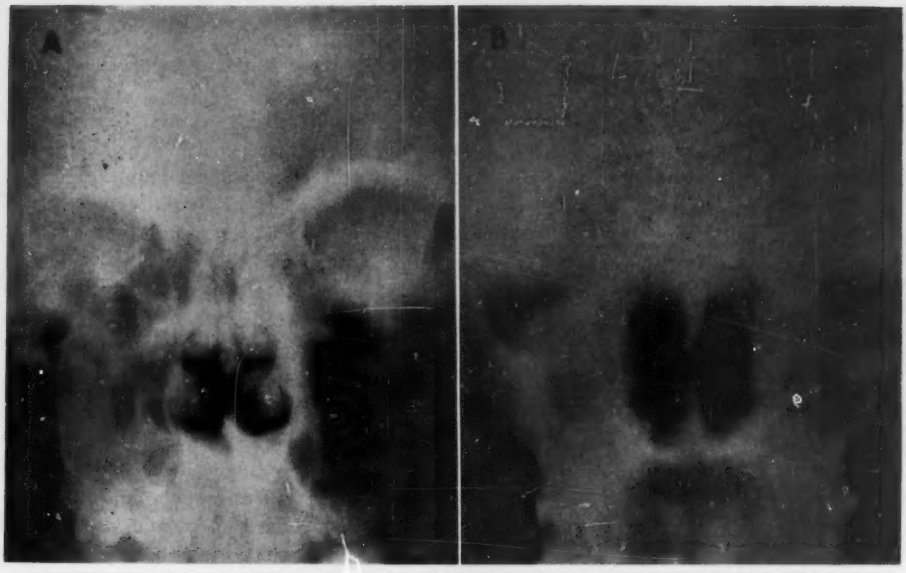

Fig. 10.—Paranasal sinus tomography. *A*, normal tomograms at 5 cm. levels. The nasal septum, turbinates, and medial walls of the maxillary sinuses are intact, as is the nasal septum. *B*, tomograms of Case 121 at 5 cm. levels demonstrate the striking absence of turbinates and loss of bone structure in the nasal septum and medial walls of the maxillary sinuses. Removal of a nasal polyp was the only surgical procedure performed on this patient.

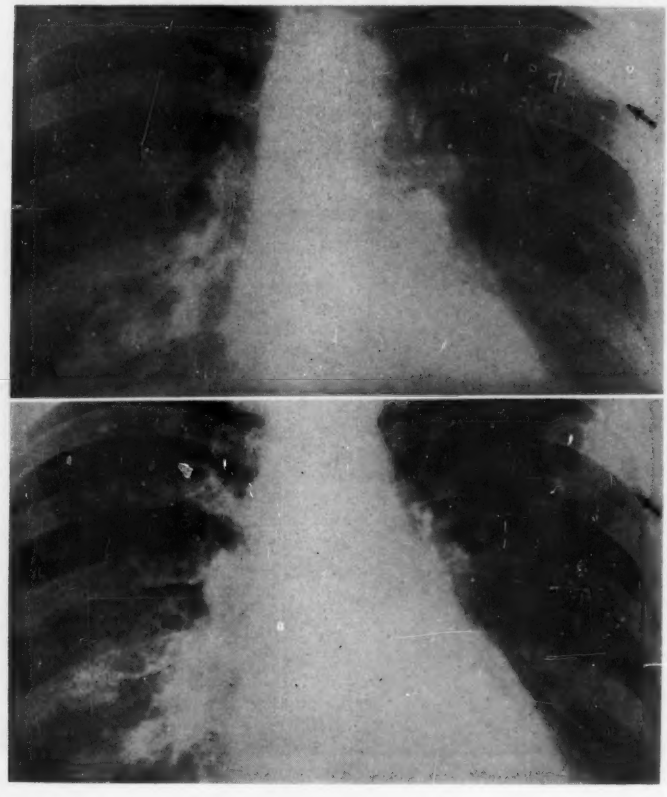

Fig. 11 (Case 122).—*A*, chest film taken on Sept. 28, 1953. Pulmonary nodular lesions appearing within a three-month period after normal chest film, during the stage of active disease. There is a 3×2 cm. circumscribed lesion in the left upper lobe (arrow) and a 1 cm. nodule in the right lower lobe overlying the rib along the right paracardiac border. *B*, Oct. 19, 1953. There is progressive increase in size of the lesions with cavitation of the left upper lobe nodule.

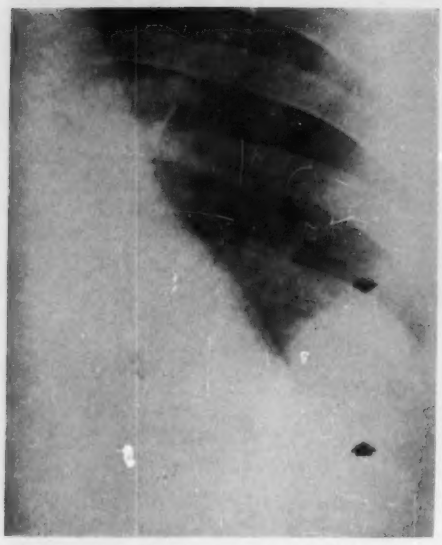

Fig. 12 (Case 121).—The chest x-ray taken on Dec. 16, 1953, shows a 7×8 cm. left lower lobe circumscribed mass.

ular densities which simulate metastatic neoplasm in their smooth, round shape. They appear relatively suddenly (six weeks, Case 122), grow rapidly, and may undergo central necrosis and cavitation (Figs. 11 and 12). The fate of these lesions will be described in the therapy section of this paper.

Renal involvement, as first described by Klinger[10] and Wegener,[26,27] is not detectable by urologic-roentgenographic methods in our case series or in the experience of others.[1-75] If the gastrointestinal tract is affected, the small bowel mucosal pattern is coarsened and segmented, as in nutritional deficiency states.[56] Arthritic manifestations are also not appreciated on films, since there are no bone changes.

Identifying Pathologic Characteristics

It was Wegener[26,27] who recognized that the pathologic changes in this disease did not correspond to any of the known granulomata of specific etiology and also differed from the "ordinary forms of periarteritis nodosa." Thus the cases in the literature—carefully described and documented as lethal midline granuloma, or Wegener's granuloma—as well as those from University Hospital, are characterized by three pathologic features, no one or two of which, in the absence of the others, are dominant anatomically[26,27,106]:

1. Necrotizing granulomatous lesions in the upper respiratory tract or in the lower respiratory tract or in both[26,27,106] (Figs. 13 and 14).

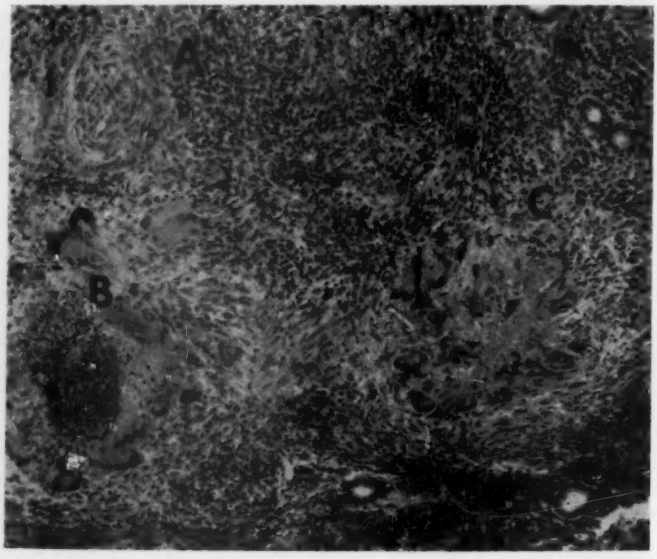

Fig. 13 (Case 115).—Nasal turbinate. *A*, small artery with arteritis and extravascular inflammation and necrosis. *B* and *C*, sharply circumscribed granulomatous, necrotic foci illustrating pseudotubercle formation. Both are surrounded by discrete groups of epithelioid macrophages. Focus *B* has a suppurative center, while Focus *C* has a fibrinoid center. The latter has the appearance of a "rheumatoid nodule," which is seen in other hypersensitivity states. Hematoxylin and eosin; reduced 15% from mag. ×80.

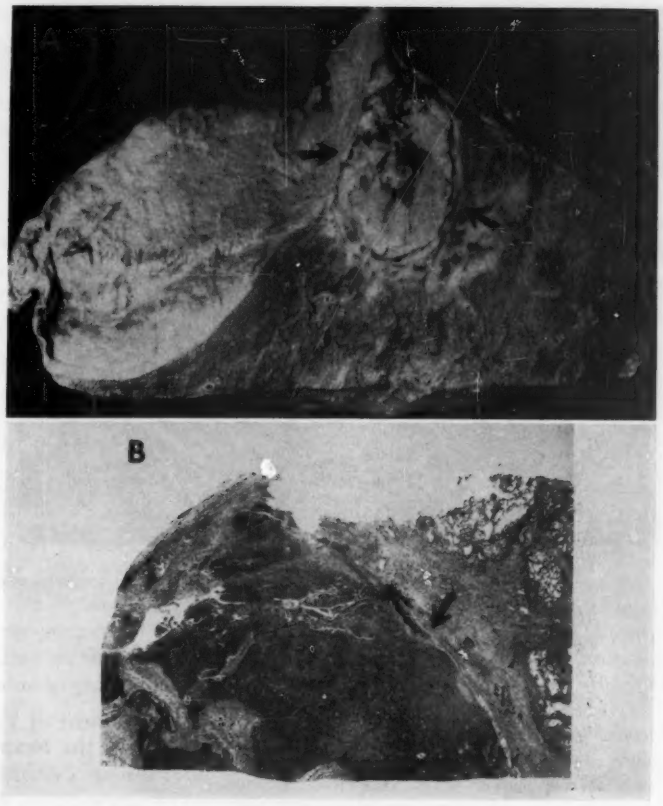

Fig. 14 (Case 121).—Granuloma of the lung. *A*, gross specimen, demonstrating a large circumscribed granuloma (arrows) in the lower lobe of the left lung (compare with Fig. 12). *B*, microscopic section through the pulmonary granuloma, demonstrating central coagulation necrosis. Hematoxylin and eosin; reduced 15% from mag. × 5.

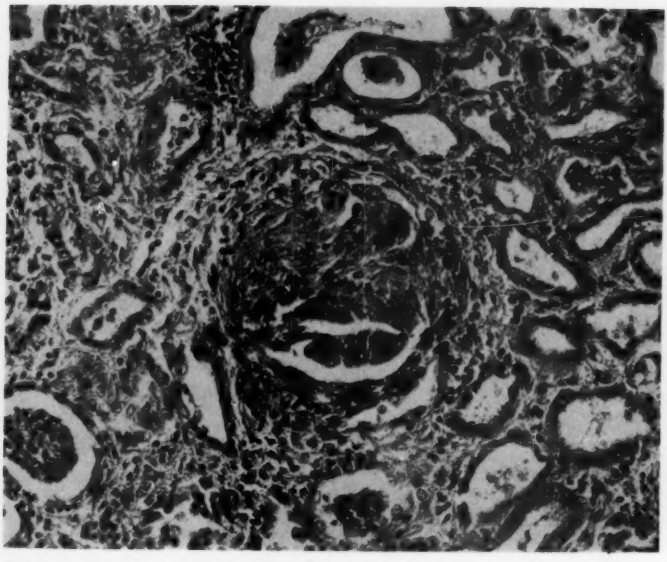

Fig. 15 (Case 121).—Kidney. Glomerulitis with fibrinoid necrosis and inflammation. There is also periglomerular inflammation of Bowman's capsule. Hematoxylin and eosin; reduced 15% from mag. × 130.

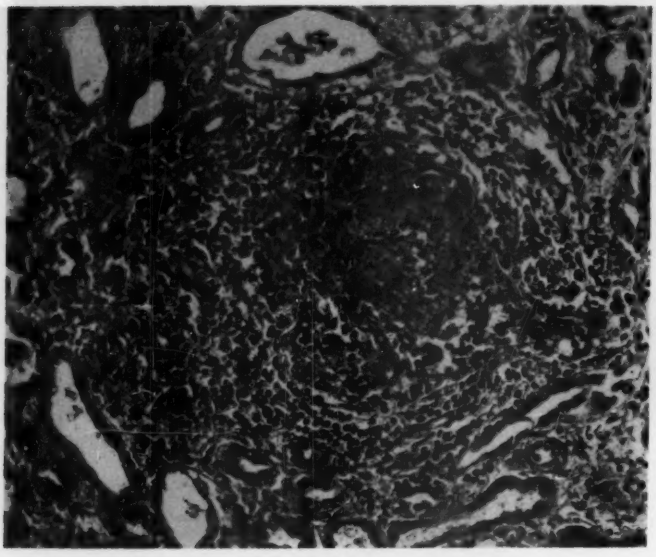

Fig. 16 (Case 121).—Kidney. Early granuloma formation. Marked periglomerular exudative reaction in a destroyed glomerulus. The granuloma is surrounded by a rampart of radiating cells as described by Wegener. Hematoxylin and eosin; reduced 15% from mag. × 130.

2. Glomerulitis, characterized by necrosis and thrombosis of loops or lobes of the capillary tuft, capsular adhesion, and ultimate evolution as a granulomatous lesion[20,27,31,35,37,49,107,108] (Figs. 15 and 16).

3. Generalized focal necrotizing vasculitis involving both arteries and veins[21] in the upper and lower respiratory tracts as well as in distant organs, such as the spleen, heart, esophagus, intestine, ovary, cervix, and integument (Fig. 17). Disseminated granulomata are also to be found in these organs.[35,50]

A more complete description and discussion of these pathologic findings will be presented in a subsequent publication.

Management of Fatal Granulomatosis of the Respiratory Tract

Various Chemicals, X-Ray, Surgery.—The medicaments for the treatment of this

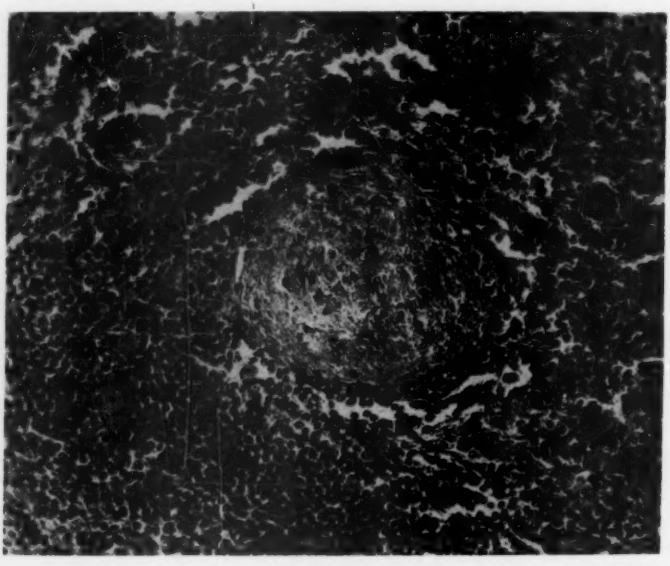

Fig. 17 (Case 120).—Spleen. Granulomatous trabecular arteritis with central fibrinoid necrosis.

disease have varied from the use of heavy metals and nitrogen mustards through radium and roentgen-ray therapy to the antibiotics and the steroid hormones. The various inorganic and organic chemicals have done virtually nothing to allay the disease. The employment of radium therapy and x-irradiation has not permanently arrested the disease process. Those patients who responded to the antibiotics and were "cured" turned out to have specific infective granulomas. Sixty-three patients in this series had various surgical procedures varying from a simple biopsy through radical operations on the nose and paranasal sinuses to thoracic surgical and other procedures (Table 11). Such operative interventions usually did not cure the disease but appeared to provide a stimulus for progression of the lesions—exacerbation of the disease, shocking deformity, systemic spread, and death. The exception is the survival of one patient in the University of Michigan Medical Center series (Case 124).

TABLE 11.—*Surgical Procedures Performed on Sixty-Three Patients with Fatal Granulomatosis of the Respiratory Tract*

(*a*) Types of procedures	
Otolaryngological procedures	(Total, 66)
Nasal polypectomy	4
Turbinectomy	2
Excision of furuncle of nasal vestibule	1
Submucous resection of nasal septum	8
Debridement of necrotic tissue of nose	3
Removal of granulation tissue from nose	1
External frontoethmoidectomy	14
Caldwell-Luc	16
Denker	1
Antrotomy	7
"Maxillary sinus operation"	5
Maxillary sinus irrigation	1
Tonsillectomy	1
Mastoidectomy	2
Oral surgical procedures	(Total, 3)
Tooth extractions	3
Thoracic surgical procedures	(Total, 4)
Exploratory thoracotomy for pulmonary nodular densities	1
Incision & drainage of pulmonary granuloma	1
Lobectomy for bronchiectasis & granuloma	2
Other surgical procedures	(Total, 3)
Arthrotomy (knee joint)	1
Excision of granuloma of skin (in cholecystectomy scar)	1
Hip (acetabulum) operation	1
	Grand total, 76
(*b*) Clinical course of patients who had surgical procedures	(Total, 63)
Dead	51
Not getting better, but fate not known	9
Living	
Alive & well 10 yr. (1959); Case 124	1
Alive with remission; Case 104, 5 mo.; Case 103, 8 mo.	2

Adrenal Cortical Hormones.—The adrenotropic and adrenocortical hormones have provided the physician with the best available tools to date, not only for treatment but also for scrutiny of the pathogenetic implications that can be drawn from such therapy. Their use in pharmacologically effective dosage may alter the destructive granulomatous process of this disease. The changes observed radiographically and histologically in the lungs are very dramatic (Fig. 18). Clinically, the evidence of renal damage heralded by hematuria, albuminuria, and cylindruria may disappear. Although the granulomatous process in the upper respiratory tract appears to respond clinically, the evidence of continued cartilage and bone destruction in the midfacial region is noted on serial x-ray films and histologic studies suggest that only the rate of tissue destruction is altered. *However, steroid therapy has had the effect of preventing slough of large midfacial tissue areas, thereby obviating the facial deformity and exsanguinating hemorrhage which were formerly associated with this disease (Fig. 19).*

When these agents are used, all efforts are directed toward obtaining maximal therapeutic benefits while minimizing the hazards attending chronic corticoid administration (Table 13). A procedural pattern has been developed which increases the possibility of attaining these goals:

1. Steroids should be started in maximal, effective dosage in order to obtain prompt control of the disease. The amount is then rapidly reduced stepwise to the lowest practicable maintenance dose per day.

2. The increased potency relative to hydrocortisone of synthetic corticoids like prednisone requires awareness that the incidence of therapeutic complications is largely proportional to the hydrocortisone (therapeutic anti-inflammatory potency)

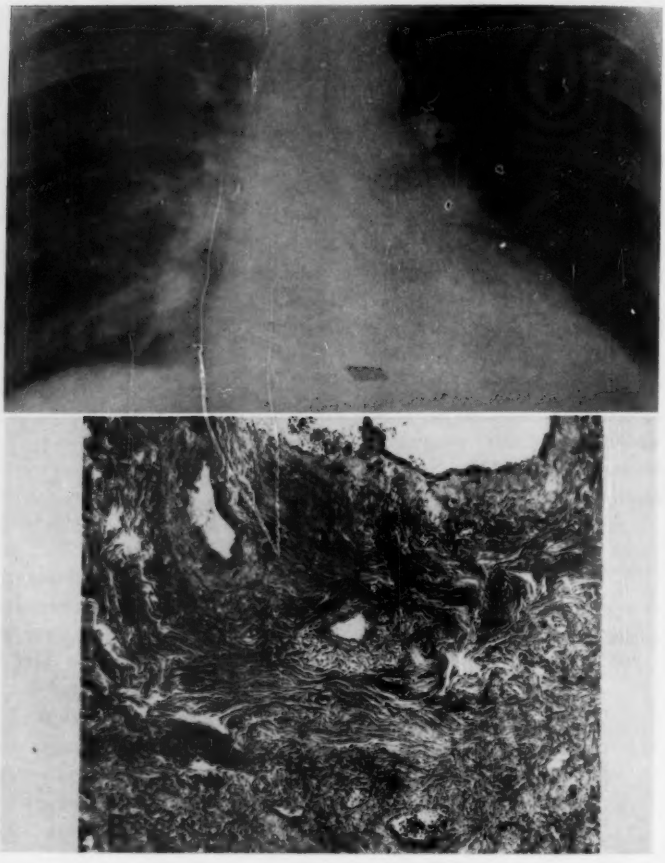

Fig. 18 (Case 122).—*A*, chest x-ray taken in January, 1956, twenty-six months after onset of corticosteroid therapy. Comparison with Figure 11 reveals complete resolution of the nodular pulmonary lesions observed in the pretreatment period, except for subpleural scarring in the left upper lung field. *B*, histologic section (post mortem) of subpleural scar seen above. No evidence of granuloma was found in the lungs. Hematoxylin and eosin; reduced 15% from mag. ×85.

equivalent given daily and not to the "smaller dosage" actually prescribed (Table 12).

3. If large amounts of steroids must be continued indefinitely, specific adjuvant therapy helps reduce the incidence and soften the impact of the inevitable "side-effects" of treatment.

For most diseases, including fatal granulomatosis of the respiratory tract, 200 mg. of hydrocortisone or its equivalent is an effective initial daily dose. Once symptomatic control is attained, an attempt is usu-

TABLE 12.—*Therapeutic (Anti-Inflammatory) Potency, Compared to Hydrocortisone, of Natural and Synthetic Adrenocorticosteroids in Current Use*

Substance	Synonym	Therapeutic Potency	Suppressive Therapeutic Dosage, Mg/Day	Electrolyte Effects of Therapeutic Amounts
Corticotropin	ACTH	3	80 *	++++
Hydrocortisone	Compound F	1	200	++
Cortisone	Compound E	4/5	250	++
Prednisone	Meticorten	4	50	—
Prednisolone	Meticortelone	4	50	—
Methylprednisolone	Medrol	5	40	—
Triamcinolone	Aristocort Kenacort	5	40	—
Dexamethasone	Decadron Deronil	25	8	—

* Dosage in clinical units instead of mg.

Fig. 19.—The value of steroid therapy in maintenance of midfacial tissue integrity. *A* (Case 119), facial deformity prior to death. No corticosteroids available. *B* (Case 122), facial appearance prior to death; moon facies of hyperadrenalism. Ocular complications unchecked in spite of corticotropin and cortisone. *C* (Case 121), facial appearance prior to use of newer anti-inflammatory corticoids (prednisone). The patient had been on 40 units of repository corticotropin injection and 50 mg. of Compound E for five months. *D* (Case 121), facial appearance after two years of prednisone therapy. The facies of hyperadrenalism are absent.

TABLE 13.—*Metabolic Complications Attending Prolonged High-Dosage Administration of Adrenal Steroids*

Metabolic Effects	Clinical Manifestations	Prophylactic or Therapeutic Measures
Protein catabolism	Muscle wasting (thin arms & legs; pot belly; weakness)	Diet: high protein (100-110 gm.) Quart of milk or equivalent daily
	Osteoporosis (back pain; vertebral collapse; rib fractures, etc.; renal calculi)	Vitamin D: 1 capsule (50,000 units) daily
	Ease of bruising	Testosterone cyclopentylpropionate, I.M., every 3 wk.
	Purple striae	Men: 200 mg.
		Women: 100-150 mg.
		Diethylstilbestrol, orally
		Women: 1 mg. daily first 20 days of each month
		Men: 0.5 mg. every other day or daily first 20 days of each month
Anti-insulin action & gluconeogenesis	Glycosuria	Diet: 200 gm. carbohydrate
	Diabetes mellitus	Insulin: isophane (NPH) or lente, once daily
Retention of sodium & water; potassium loss in urine	Edema	Diet: 800 mg. sodium (2 gm. salt daily)
	Hypertension	Potassium chloride: 2 gm. t.i.d. with meals
	Hypokalemia	
Deposition of fat	Moon facies	——
	Buffalo hump	
Androgenic effects	Hirsutism	Partially nullified by estrogen used in antiosteoporosis regimen
	Acne	
	Amenorrhea	
Suppression of pituitary-adrenal axis	Acute adrenal insufficiency if steroids stopped or if superimposed stress	Hydrocortisone sodium succinate
		Prophylaxis: 50 mg. I.M. q. 6 hr.
		Treatment: 25 mg. I.V. immediately; 10 mg/hr. by continuous I.V. infusion in 5% dextrose in saline or water.
Anti-inflammatory action	Dissemination of tuberculosis or other infection	Prophylaxis vs. tuberculosis
		Isoniazid, 100 mg. t.i.d.
		Potassium *p*-raminosalicylate, 3 gm. q.i.d.
		Antibiotics as indicated
Stimulation of gastric secretion	Peptic ulcer	Prophylaxis & medical treatment
	Massive gastrointestinal hemorrhage, perforation of bowel	Diet: 6-feeding bland
		Antacids, e.g., aluminum hydroxide (Amphojel) 8 cc. 5 times daily between feedings
		Phenobarbital, 32 mg. t.i.d., a.c.
		Atropine, 1/150 grain (0.4 mg.) or propantheline (Pro-Banthine), 15 mg. t.i.d., a.c.
		Surgical intervention as last resort
Stimulation of cerebral cortex	Insomnia	
	Euphoria	
	Toxic psychosis	Discontinue steroids as rapidly as possible

ally made to reduce maintenance dosage to not more than 50-60 mg. of hydrocortisone per day. However, this disease is usually not completely suppressed by corticoids, and the equivalent of 200 mg. of hydrocortisone may have to be continued daily to sustain maximal retardation of the downhill course.

The hydrocortisone equivalent of a corticoid compares its potency to that of hydrocortisone with respect to three inseparable biologic properties. The paramount one is its anti-inflammatory activity, since this property fundamentally determines its therapeutic effectiveness. Directly proportional to the antiphlogistic potency, however, occur "glucocorticoid effects" manifested by protein wasting and carbohydrate intolerance, and suppression of corticotropin (ACTH) secretion by the anterior pituitary. In Table 12 are compared the hydrocortisone equivalents of all compounds now in clinical use. Since the synthetic corticoids (prednisone, prednisolone, methylprednisolone [Medrol], triamcinolone [Aristocort, Kenacort]) are four to five times more potent than hydrocortisone, weight for weight, 50 mg. of prednisone

or 40 mg. of methylprednisolone daily is as therapeutically beneficial as 200 mg. of hydrocortisone. Only 8 mg. of the much more potent dexamethasone (Decadron or Deronil) exerts a similar effect. Simultaneously, however, these dosages tear down body protein, predispose to hyperglycemia, and suppress the pituitary gland with the force of 200 mg. of hydrocortisone.

On the other hand, as shown in Table 12, the synthetic agents from prednisone on down offer the prime advantage over the natural steroids of exerting only minimal electrolyte effects in the ordinary dosage range. Sodium and water retention and urinary potassium loss are usually negligible. Since serious complications, like edema, hypertension, and hypokalemia, are thereby largely avoided, prednisone and its successors are in general the therapeutic agents of choice. But intramuscular hydrocortisone or corticotropin may be indicated if the beneficial effects of the steroid analogues wear off, since in some cases the natural compounds are therapeutically more effective than the artificial ones.

Complications of Corticoid Therapy.—Because the patient with this disease must continue on large amounts of steroids indefinitely, one or more of the complications listed in Table 13 will eventually occur. Some of these are more serious than others. For example, although the characteristic moon facies and buffalo hump of Cushing's syndrome are cosmetically undesirable, they are asymptomatic and benign. Androgenic effects like hirsutism and acne are also relatively minor and discountable sequelae when steroid therapy is used. Conversely, each of the other complications in Table 13 constitutes a threat to the patient's life. In the hope of blunting their impact, prophylactic therapy is directed against these latter complications.

The crippling effects of chronic protein loss are combatted by an antiosteoporosis regimen consisting of diet, vitamin D, and sex hormones. This program is started immediately. The diet is high in protein (100-110 gm.), including a quart of milk daily for its combined protein and calcium content. Vitamin D in 50,000 unit capsules given daily promotes absorption of calcium from the intestinal tract. The protein-building effect of androgens is utilized by giving testerone cyclopentylpropionate (Depo-Testosterone) intramuscularly every three weeks; 100-150 mg. to women and 200 mg. to men. An estrogen is also prescribed to stimulate osteoblastic formation of new bone. Diethylstilbestrol is cheap and effective and is administered to women cyclically as 1.0 mg. daily for the first 20 days of each month to permit withdrawal bleeding if endometrial response is excessive. The dose for men is 0.5 mg., taken either the first three weeks of every month or every other day continuously. Combined androgen-estrogen administration usually reduces unwanted masculinizing effects in women and feminizing traits in men. This antiosteoporosis regimen may seem cumbersome at first glance, but it uniformly prevents skeletal decalcification and fractures and is hardly ever complicated by renal stone formation.

Steroid-induced diabetes mellitus generally occurs only in patients of diabetic heritage.[128] It is easily controlled by limiting carbohydrate intake to 200 gm., restricting calories in obese patients, and prescribing a single dose of isophane or lente insulin daily before breakfast. Insulin is required because diabetes flared by steroids does not respond to oral hypoglycemic compounds like tolbutamide (Orinase).

Depression of the pituitary adrenocortical axis is a dangerous sequela of corticosteroid therapy. Unable to combat the stress of infection, surgery, or trauma by automatically increasing his adrenal output of hydrocortisone, the patient may collapse from adrenal failure manifested as irreversible shock, leading to death if untreated. Even without superimposed stress the same thing can occur if steroid therapy is suddenly stopped. For example, if administration of oral corticoids is interrupted by anorexia caused by progression of the granulomatous disease, adrenal insufficiency will

shortly follow unless parenteral steroids are given. The preparation of choice is soluble hydrocortisone (hydrocortisone sodium succinate), 200 mg. daily given intramuscularly, to prevent adrenal crisis and intravenously to treat it. If a surgical emergency arises, oral therapy is stopped 12 to 18 hours preoperatively and hydrocortisone sodium succinate is started, 50 mg. intramuscularly every six hours throughout the surgical and postoperative period until the patient can resume oral medication. If an acute febrile illness precipitates adrenal crisis, the same compound is given intravenously, 25 mg. immediately and 10 mg. per hour in a continuous daily infusion of 2,000 cc. of 5% dextrose in water or saline until the patient can eat again.

The anti-inflammatory activity of adrenal corticosteroids which is therapeutically exploited is not only potent but also nonspecific. It blocks the inflammatory response of the body to infectious processes generally. However, administration of the chemotherapeutic and antibiotic agents checks the progress of specific bacterial infections should these occur.

Ulceration of the gastrointestinal tract is a doubly dangerous complication of steroid therapy. It usually appears alarmingly as profuse hematemesis or melena or as a perforated ulcer in the stomach or small bowel. However, the diagnosis of perforation may be irreparably delayed if the lesion is painless, because normal peritoneal inflammatory response has been blunted by steroids. Generalized peritonitis may subsequently overwhelm the patient. Fortunately, steroid-induced ulcers tend more to bleed than perforate. As in our experience, it has been recently reported [109] that such hemorrhages have responded to the standard conservative measures (six-feeding bland diet, antacids, sedation, and autonomic blocking agents such as atropine), even when corticoids were continued to maintain control of the primary disease.

Toxic psychoses precipitated by steroids often appear as hyperexcitable manifestations of frankly manic states. This alarming complication is more easily prevented than treated. Relatively strong therapeutic indications are demanded before prescribing these compounds to patients with extreme emotional lability or a past history of psychic disturbance. In addition, the use of corticotropin without limiting salt intake and administration of potassium supplements is more often complicated by psychic changes than any other steroid program. This suggests that intracerebral electrolyte shifts potentiate the basic cerebrocortical excitation caused by hydrocortisone. Psychoses are thus largely avoided by choosing an agent other than corticotropin or by restricting salt and adding potassium if corticotropin is used.

The retention of sodium and loss of potassium can be avoided by using the synthetic steroid compounds. With ordinary suppressive doses of 40-50 mg. daily of prednisone, 32-40 mg. of methylprednisolone or trianicinolone or 8 mg. of dexamethasone, dietary salt restriction and potassium supplements are not needed. When corticotropin is used, however, one must limit daily intake of sodium to 800 mg. (2 gm. of salt) and give added potassium to offset renal losses. When glomerular function is adequate (normal BUN or NPN), 6 gm. of potassium chloride is given daily in divided doses with meals. If the NPN is elevated, periodic serum potassium determinations will indicate whether supplements are needed. Although cortisone and hydrocortisone cause less intense electrolyte shifts than corticotropin, one should also restrict salt and add potassium when they are prescribed for long periods of time.

Corticotropin was used initially in two of our patients (Cases 121 and 122) who were treated most vigorously and uninterruptedly with corticoids. From the beginning, both were on the antiosteoporosis regimen, salt restriction, and potassium supplements. Within three months, each patient had the round face, cervicodorsal fat pad, hirsutism, and acne of Cushing's syn-

drome, but neither ever developed edema, and Case 121 was always normotensive. Preexisting mild hypertension in Case 122 became moderately severe during treatment and may have contributed ultimately to her death following coronary occlusion. She also developed a bleeding peptic ulcer which healed rapidly on medical management despite continued steroid administration. This patient obviously sustained many severe complications of chronic high-dosage corticoid therapy in spite of intensive prophylactic measures, and one might wonder if treatment was worthwhile in the long run. It therefore bears emphasis that the patient literally rose from the death bed and lived an additional 30 months on continuous steroid treatment. During this time she was spared the immobilizing sequelae of protein destruction, namely, muscle wasting with physical weakness, vertebral collapse, and similar skeletal fractures. Case 121 lived only 11 months after corticotropin was started, during which time he showed no overt evidence of protein wasting while receiving an average of 80 units of repository corticotropin injection (Acthar Gel) daily. This neutralization of the protein catabolic effects of steroids duplicated our experience with carefully planned steroid regimens for other diseases requiring long-term administration of corticoids.

Pathogenesis of Fatal Granulomatosis of the Respiratory Tract

The Question of Pituitary and Adrenal Cortical Deficiency

In a discussion of the etiology and pathogenesis of this bizarre disease it is suggested, "relative pituitary or adrenal cortical dysfunction . . . a relative deficiency of . . . the secretion of . . . compound 'E' of Kendall (cortisone)" may be the underlying cause of this unique granulomatous lesion.[42]

Studies of adrenal cortical function in two of the patients in this series (Cases 121 and 122), however, plus clinical data from their patients in the present series and from published reports[45,52,57] make it extremely unlikely that adrenal deficiency is causally related to this granulomatous disease.

The existence of *primary* adrenal insufficiency, i.e., failure of the adrenal cortices themselves, is quickly ruled out by studying the responses to corticotropin as exhibited by Cases 121 and 122 (Table 14). In each case a sharp rise in urinary 17-hydroxy corticosteroids and 17-ketosteroids proved that adrenal responsiveness and reserve were intact. Moreover, the pretreatment 17-ketosteroid excretion by Case 121 does not support the concept that idiopathic anterior pituitary failure with *secondary* adrenocortical deficiency is the cause of this disease. The baseline value of 14.9 mg. per day signified normal adrenal function during the florid stage of granulomatosis. In addition, laboratory evidence of normal gonadal and thyroid function was further evidence against anterior pituitary deficiency.

Although adrenal hypofunction cannot be invoked as the cause of fatal granuloma of the respiratory tract, cortical collapse might conceivably occur as a *result* of

TABLE 14.—*Urinary Excretion of Steroids Before and During Treatment with Corticotropin* *

Case	Age	Sex	17-Ketosteroids †		17-Hydroxycorticosteroids ‡	
			Before Therapy	During Therapy	Before Therapy	During Therapy
121	35	M	10-20 14.9	50 or more 93.7	3-10 —	20 or more 19.7
122	50	F	8-15 3.7	40 or more 61.2	2.5-8.0 —	20 or more 28.1

* Mg/24 hr.
† Modified Callow & Callow method.[158]
‡ Porter-Silber method.[188]

granulomatous invasion of the anterior pituitary and thus contribute to the characteristic terminal "exhaustion." For example, in Case 122, who was moribund and manifesting what Williams[42] termed "Addisonoid symptoms" before corticotropin was started, the low pretreatment 17-ketosteroid value of 3.7 mg. per day might have been due to adrenal deficiency. However, even with normally functioning adrenals, urinary 17-ketosteroids and 17-hydroxycorticosteroids are invariably low in chronic cachectic states like anorexia nervosa and terminal malignancy[110] because of impaired hepatic conversion of circulating hydrocortisone to its excretory products. That this latter explanation for low steroid excretion applied to Case 122 was supported by the postmortem finding of an intact sella turcica and absence of granulomatous lesions in the pituitary gland. In Case 121, likewise, necropsy confirmed that the sella turcica and its contents were intact. Postmortem examinations on other patients in our series and those reported in the literature showed that in no instance was the pituitary gland or hypothalamus encroached upon by the granulomatous process.

A final point against the thesis that adrenocortical deficiency is related to any important extent to this disease is the dosage of steroids required to check the progression of the granulomatous lesions. In undisputed cortical failure such as is seen in Addison's disease, only small physiologic doses, 5-10 mg. of repository corticotropin injection or 15-30 mg. of cortisone or hydrocortisone daily, constitute adequate replacement therapy. In contrast, the three patients in this series for whom steroids were prescribed required the same excessive, pharmacologic amounts—100 to 120 units of repository corticotropin injection or 200 mg. of cortisone daily—which are needed to effect symptomatic improvement in many disease states where no question of adrenocortical failure arises.

The Question of Hypersensitivity Reaction

The search for a specific infectious agent, as it has been pursued by these and other authors, has yielded only a mixed flora usually found in the upper respiratory tract or as contaminants. The clinical and pathologic features are such that they represent a disease process to the exclusion of specific infective granulomas and certainly neoplasms. This disease has many of the features which are characteristic of human hypersensitiveness. By careful consideration of the clinical data and by comparative study of the pathologic anatomy of this type of necrotizing granulomatous angiitis and analogous vascular and granulomatous lesions, both human and experimental evidence for considering the lethal midline granuloma-Wegener's granuloma complex a disease of hypersensitivity is presented.

What Is Hypersensitivity?—A common disturbance in immunity is that of hypersensitivity. The accepted basis on which all manifestations of hypersensitivity depend is the combination of antigen with its specific antibody. Some of these changes are temporary, leaving no recognizable after-effects. An example is the wheal and flare of urticaria. Others are slower in onset and leave more permanent change, such as lesions of polyarteritis[110-114] or the Arthus phenomenon.[115-118] *It is this pathologic alteration of the tissues of the host which characterizes the immune or defensive reaction as hypersensitive.*

Types of Antigens Which Can Be Responsible.—1. Atopic Allergens Such as Pollens, Other Inhalants and Foods: The pathology of atopic disease is characterized by a marked but usually transient edema of tissues. The cellular inflammatory reaction is often rather meager, and necrosis and granuloma formation rarely occur. Clinically, too, the intermittent or fluctuating character of atopic diseases stands in marked contrast to the usually progressive course of this fatal granulomatous disease. Thus atopic antigens may be regarded as

rather unlikely candidates for a primary etiologic role in the pathogenesis of this disease.

2. Foreign Sera and Drugs: In both man and experimental animals it is known that vascular lesions can be produced by hypersensitivity reactions to these agents. This possible etiologic factor should be considered—particularly in patients with a disease associated with generalized vascular lesions. Were foreign sera commonly of etiologic importance, however, this would have been readily apparent in the cases previously investigated and those reported by the authors. Drug allergy cannot be dismissed quite so readily, since patients' histories may not be reliable in this respect. On the other hand, although drug allergy might well produce some type of disseminated vasculitis, granuloma formation would be unusual (except at injection sites). It also would be hard to understand why the systemic administration of a drug would produce a biological granuloma in the respiratory tract.

3. Infectious Agents: (*a.*) Localized infection. The clinical-pathological features of this disease are such that one's first thought is a tissue hypersensitivity reaction evoked by the local invasion of some known pathogen—bacterial, viral, rickettsial, mycotic or parasitic. No specificity of the granuloma in relation to any known pathogen has been found. However, the possibility that they may play a part will be discussed under tissue autoantigens below.

(*b.*) Generalized intermittent or distant infections. It is possible that this disease process is initiated by a local infection, but having sensitized the tissues, the etiologic agent locally or temporarily may be eradicated, thus accounting for failure to recover the organism from the tissues at a later date.

4. Contact Allergens: Although there appears to be little similarity between this granulomatous disease and contact type hypersensitivity, the allied phenomenon of a foreign-body reaction should receive consideration, be this reaction on an immunologic basis or not. Although the presence in tissues of a number of foreign unabsorbable materials can give rise to granuloma formation, the progressive nature of this granulomatous lesion would suggest the continuing presence of any such foreign bodies. Yet, none have been identified in pathologic material examined to date.

5. Tissue Autoantigens: It is possible in the pathogenesis of fatal granulomatosis of the respiratory tract that there is initially a local tissue injury by some noxious substance as a chemical irritant, a physical agent, or an infectious organism—particularly the latter. The altered host tissue then might act as foreign and stimulate the formation of autoantibodies. The interaction of these antibodies with the particular tissue area would result in an inflammatory reaction which might lead to more altered tissue. Thus a vicious cycle could be established within the tissues of the respiratory tract. These tissues would possess a predilection for union with such antibody. This union results in more damaged tissue, which in turn finds its way via the circulation to antibody-forming centers such as the spleen and even the kidney,[119-123] resulting in more antibody. *Support of this is found in the observation that surgical procedures performed in the involved tissue area or in another part of the body (Table 2) in most instances results in a rapid downhill clinical course.* This probably occurs when sufficient antigen (damaged tissue) is made accessible to the major antibody-forming centers. The well-known vast difference in the capacity of humans to not only form antibodies but also evoke the hypersensitive state is in agreement with (1) the individual differences in the duration of the clinical picture and (2) the observation that relatively few people are found to become ill with this progressively fatal granuloma.

Further evidence for the autoimmune concept of pathogenesis may be found in the universal serologic pattern of Kahn,[124,125] where a serologic precipitation reaction is the result of particular lipids liberated in the tissue destructive processes of a particular disease. These lipids call forth homologous autoantibodies which react with corresponding lipids present in the Kahn antigen. The intensity of the precipitation is apparently closely related to the activity of the disease. When the activity is low, the intensity is low; when the activity is increased, the intensity of precipitation is increased. *The exception to this observation is noted when the activity of the disease is so marked as to overwhelm the patient (Fig. 20).*

Thus hypersensitivity reaction evoked by an autoantigen-antibody mechanism would appear to be the most probable mechanism in the etiology and pathogenesis of this disease. This type of mechanism has also been implicated for nonspecific inflammatory diseases, such as systemic lupus erythematosus [126] and rheumatoid arthritis.[127] Further carefully planned immunologic studies will test the validity of this proposition.

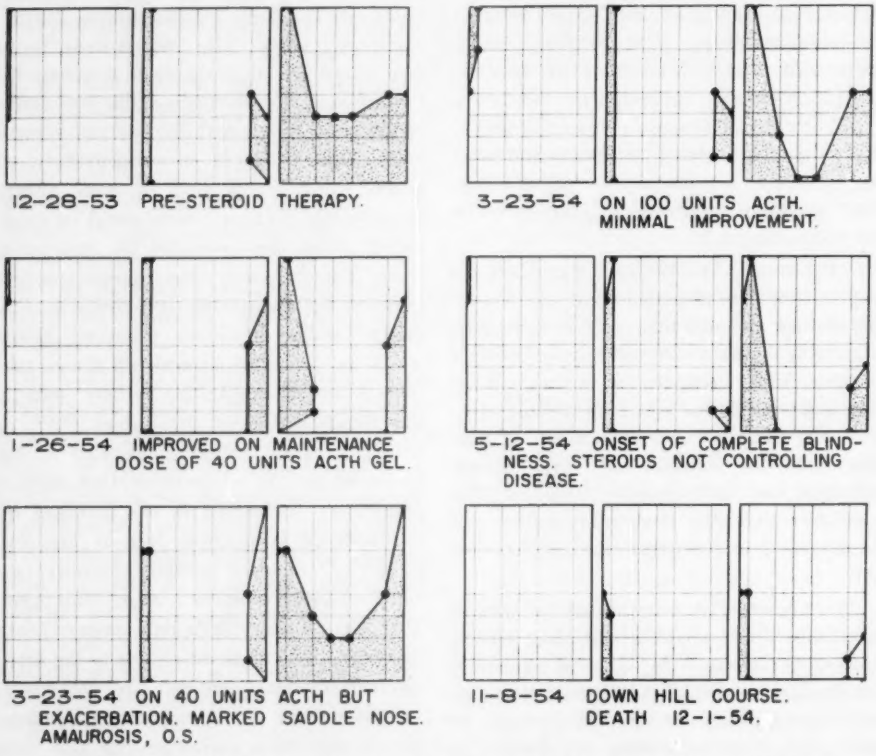
12-28-53 PRE-STEROID THERAPY.
3-23-54 ON 100 UNITS ACTH. MINIMAL IMPROVEMENT.
1-26-54 IMPROVED ON MAINTENANCE DOSE OF 40 UNITS ACTH GEL.
5-12-54 ONSET OF COMPLETE BLINDNESS. STEROIDS NOT CONTROLLING DISEASE.
3-23-54 ON 40 UNITS ACTH BUT EXACERBATION. MARKED SADDLE NOSE. AMAUROSIS, O.S.
11-8-54 DOWN HILL COURSE. DEATH 12-1-54.

Fig. 20 (Case 121).—Universal serologic reaction (Kahn) as indicator of autoantibody activity. Three graphs are presented for each serologic precipitation reaction run on given dates. The left graph of each serum specimen tested is based upon the readings of precipitation results without incubation (immediate reading). The center graph represents reaction after 4 hours; the right graph, after 24 hours. All readings are at icebox (5 C) temperature. The abscissa of each graph represents the per cent NaCl used in the seven dilutions: 0, 0.15, 0.6, 0.9, 1.2, 1.8, and 2.1. The ordinate represents the seven serum dilutions: undil., 1:2, 1:4, 1:8, 1:16, 1:64, and 1:256. Most significant precipitation reaction is noted in the 24-hour incubated specimens.

Summary and Conclusions

Data on 124 cases of lethal midline granuloma-Wegener's granulomatosis are presented—112 from the medical literature and 12 from the University of Michigan Medical Center.

It is suggested that the rhinopharyngologic-midfacial disease described by Stewart [13] and the rhinologic-systemic syndrome described by Wegener [26,27] are one and the same disease process—a granulomatous necrotizing angiitis, primary in the respiratory tract with systemic involvement and invariably fatal.

Through concentration of case material it has been possible to formulate the clinical manifestations of the period of active disease and to observe the effects of various methods of treatment.

Surgical intervention appears to increase the morbidity and intensity of the ulceronecrotic destructive process in the midfacial and other areas of the body, thereby creating deformities shocking to behold.

When adrenal steroid therapy is used, the patients are apparently spared the frightful destruction of bone and soft tissue, particularly in the facial area, so that the face remains intact (Fig. 19). The over-all therapeutic response is usually dramatic within a few days, and it is possible to extend the lives of these seemingly doomed people by months or even years. The sequelae of chronic steroid administration are described.

The antibacterial activity of the antibiotic drugs have been invaluable in eliminating secondary invaders. Ionizing irradiation may find its effectiveness in the treatment of this inflammatory lesion.[131]

Clinical, histologic, and preliminary laboratory evidence is presented to suggest that the lethal midline granuloma-Wegener's granulomatosis complex is a hypersensitivity reaction evoked by an autoantigen-antibody mechanism.

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Case Reports from University of Michigan Medical Center

CASE 119.—A 51-year-old tool-and-die maker entered University Hospital on Feb. 6, 1946, because of a "hole on the side of the nose with pus and drainage." There was a history of "atrophic rhinitis for many years." In February, 1945, the patient noticed onset of a continuous watery to mucoid discharge. In July, 1945, six months later, the nasal discharge became purulent. There were considerable crusting, streaks of blood, and a fetid odor. The nasal symptoms were not relieved by antiseptic instillations or irrigations. The family physician removed a fragment of loose bone from the nose in October, 1945. In November, the patient developed a painful, red swelling at the inner canthus of the right eye, which did not respond to chemotherapeutic and antibiotic agents and which became gangrenous. Necrotic pieces of bone were removed, with a subsequent perforation of the indurated canthal area. Biopsy revealed inflammatory granulation tissue. X-ray therapy was advised, which the patient refused. By January, 1946, eleven months after onset of symptoms, the patient developed anorexia, weakness, lassitude, and a 15 lb. weight loss. During the patient's 25-year occupation as a tool-and-die maker, he worked with various color-painted metals, including nickel and steel, without ill effects.

Physical examination revealed a thin, chronically ill but cheerful man. The blood pressure was 120/70 (R.A.R.); temperature, 98.6 F (oral); pulse, 72 per minute and regular; respirations, 20 per minute. There was enlargement of the submandibular, axillary, and inguinal lymph nodes. The nose was filled with a profuse, purulent bloody nasal discharge and with a considerable quantity of fetid necrotic debris. After cleansing, the nasal septum was seen to have an extensive perforation with visible denuded cartilage and bone. The right middle turbinate was eroded through with a communication to the external surface of the nose via an eroded, necrotic right nasal bone and nasal process of the right maxillary bone (Fig. 3). The skin surrounding this area was intensely erythematous, with a central area of gangrenous perforation. The nasopharynx, posterior pharyngeal wall, and tonsillar pillars were covered with tenacious purulent material, which, when removed, revealed a very edematous and angry red mucous membrane surface. The remainder of the physical examination was within normal limits.

Laboratory Data on Admission.—The urinalysis was unremarkable. Blood: Kahn test was negative. The hemoglobin was 12 gm. %. The red blood cell indices were within normal limits. The sedimentation rate was 18 mm. per hour (cor.). The WBC were 5,200, with 3 band neutrophils, 61 segmented neutrophils, 23 lymphocytes, 8 monocytes, and 5 eosinophils. There were toxic granules in the neutrophils. The platelets were adequate. There was slight anisocytosis and poikilocytosis of the erythrocytes. The sternal marrow was very cellular, with active erythro- and granulopoiesis; the picture was compatible with a chronic granuloma with an active reticuloendothelial response. Skin tests were negative for histoplasmosis, blastomycosis, and coccidioidomycosis, as were skin tests for lymphogranuloma venereum and tuberculosis (OT). Specimens of nasal discharge showed Gram-positive cocci, coagulase-positive staphylococci, diphtheroids, Pseudomonas pyocyanea, Proteus, and aerobic spore-forming bacilli of soil and water group. Blood cultures were negative. Paranasal sinus x-rays showed a chronic, bilateral pansinusitis, with evidence of bone destruction. The chest roentgenograms were normal. Biopsy specimens from the nose revealed a severe, chronic purulent necrotizing nonspecific inflammation with fibrinoid necrosis of the walls of blood vessels.

Course.—The patient was hospitalized for 69 days, during which time there was a progressive downhill course. He was treated with sulfonamides and penicillin, folic acid, high-vitamin and high-calorie diet, and appropriate care of the nasal wound. The radiotherapy consultant felt that x-ray therapy would not help. During hospitalization the white blood cell count varied between 3,200 and 5,200, in spite of frequent temperature elevations up to 102 F (oral). The ulceronecrotic and gangrenous process of the nose continued its slow destructive advance to involve the entire right lateral nasal wall, bony orbit, maxillary antrum, ethmoid cells and surrounding soft tissue (Fig. 6). Blood loss associated with this shocking deformity was replaced by transfusion of whole blood. Splenomegaly made its appearance in the last two weeks of hospitalization. No other systemic manifestations were noted. The patient was taken home by his family in a state of cachexia and exhaustion, where he died on June 27, 1946—approximately 17 months after onset of illness. The cause of death recorded on the death certifi-

cate was "carcinoma of the maxillary sinuses." There was no postmortem examination.

CASE 120.—A 53-year-old sheet-metal worker was admitted to University Hospital on Dec. 30, 1943, with the complaints of "nose bleeds and choking spells." The patient was well until May, 1942, when he experienced spontaneous epistaxes two to three times a week, which were controlled by the family physician. The patient's occupation (for more than five years) necessitated breathing acid fumes. In September, 1942, there was gradual onset of nasal obstruction and formation of crusts which he could pick from the nose in large chunks. One year later, in September, 1943, the patient visited the family physician, who found "anemia," and he was treated with "concentrated liver." The patient visited the University Otolaryngological Clinic on Nov. 23, 1943, where irregular vegetative granulomatous masses were found to involve the septum and turbinates of the left nasal chamber. The mucous membranes of the right side were very hyperemic and friable. The clinical impression was carcinoma of the nose. Biopsy revealed a chronic infective granuloma with ulceration and with numerous small blood vessels suspicious of syphilis. Giemsa staining showed basophilic oval bodies which were questionable histoplasma. In December, 1943, the patient developed hoarseness, odynophagia, and dysphagia for solid foods, with dyspnea and choking spells. The latter was relieved by coughing up chunks of "soft, bloody material."

Physical examination revealed a well-nourished, well-developed and chronically ill and extremely exhausted white man. The blood pressure was 130/80 (R.A.R.); temperature, 99 F (oral); pulse, 80 per minute and regular; respirations, 20 per minute at rest. The skin and mucous membranes were very pale. There were no palpable lymph nodes. The left nasal chamber was completely filled with granulomatous tissue. The right side of the nose was very hyperemic and edematous. The nasopharynx, oropharynx, and base of the tongue were covered by a fetid, tenacious pseudomembrane, which after removal showed an angry-red mucous membrane, partially ulcerated and denuded. Mirror laryngoscopy revealed a hemorrhagic, granulomatous, ulceronecrotic process involving the vocal cords, false cords, and aryepiglottic folds, wih subglottic extension. The larynx was not fixed; the airway was barely adequate. There were hyperemia and edema of the epiglottis and pyriform recesses. There were scattered rhonchi and rales throughout both lung fields. There was a systolic murmur at the apex, not transmitted. The remainder of the physical examination was within normal limits.

Summary of Admission Laboratory Findings.—Urine: 1+ to 2+ albumin, microscopic hematuria, many granular, cellular, and hyaline casts. Specific gravity, 1.019. Blood: NPN was 43 mg. %. Kahn test was negative. Hemoglobin was 5.7 gm. %, with red blood cell indices compatible with a blood-loss anemia. WBC was 5,150 with a normal differential count; adequate platelets, and hypochromic microcytic red blood cells. Skin tests for histoplasmosis, blastomycosis, coccidioidomycosis, lymphogranuloma venereum, and tuberculosis (OT) were negative. Mouse inoculations for histoplasma and AFB (acid-fast bacilli) were negative also. Specimens of laryngeal secretions showed Gram-positive cocci, but no fungi or AFB were found. X-ray examinations revealed clouding of all the sinuses except the sphenoids, without bone destruction, and a bilateral patchy pneumonitis.

Hospital Course.—Laryngoscopy and bronchoscopy were performed in order to determine the nature and extent of the laryngotracheal granuloma. The granulomatous process extended sufficiently caudad to preclude tracheotomy. The friable nature of the tracheobronchial mucous membranes prevented adequate inspection of the tracheobronchial tree. The histologic appearance of the laryngotracheal lesion was compatible with a severe idiopathic granulomatous ulceration.

The patient deteriorated rapidly. He had frequent episodes of epistaxes and hemoptysis. Sulfonamide, blood transfusion, and oxygen therapy did not alter the downhill course. The temperature ranged from 99 to 102 F (oral). The patient developed progressive respiratory obstruction and died on Jan. 23, 1944, the 24th hospital day and 17 months after onset of illness.

CASE 121.—A 35-year-old white wild-life-conservation officer was admitted to University Hospital on Dec. 19, 1953, with the complaints of "persistent nasal discharge, aching joints, weakness, and short-windedness." The patient was in good health until May, 1951, when he developed a "cold" characterized by blood-streaked, purulent nasal discharge. There was associated brown crust formation, which the patient could pick out of the nose. The nasal secretions were so profuse that five or six handkerchiefs would be used daily. The patient visited an otolaryngologist after two weeks of the above symptoms and was told he had "an old-fashioned catarrh or atrophic rhinitis and a polyp in the left nostril." A nasal polypectomy was performed, after which the patient bled severely. There were frequent daily epistaxes, subsequently, which subsided spontaneously. Two weeks after the nasal operation the patient noticed aching knees with limitation of motion, which later involved the elbows, wrists, and fingers. There was no swelling, heat, redness, or tenderness. A diagnosis of "rheumatoid arthritis" was made. Salicylates relieved the polyarthralgia. Nasal symptoms were not relieved by

antiseptic instillations, irrigations, cautery, or systemic antibiotics. In December, 1951, the patient was started on cortisone, 25 mg. orally q.i.d., and received a total of 2,100 mg. without relief of symptoms. By November, 1952, the nasal discharge was bilateral, sanguinopurulent and more profuse. Epistaxes had increased in frequency and severity. In October, 1953, the patient had sudden, severe aching pain over the maxillary sinuses and upper teeth, associated with a "sensation of fullness in the ears," diminished hearing, and tinnitus. In November, 1953, the epistaxes continued and there were orbital pressure, pain and photophobia. He also noted dull, steady earaches, ease of fatigue, weakness, shortness of breath with mild exertion, a dry nonproductive cough, night sweats, and a feverish feeling. At no time during the patient's lifetime was there contact with mules, horses, donkeys, or other single-hoofed animals. The family history as it pertained to the patient's illness was not contributory. An older brother, also a state wild-life-conservation officer, working closely with the patient, was in good health.

Physical examination revealed that the patient appeared well nourished, well developed, and chronically ill. The blood pressure was 140/80 (R.A.R.); temperature, 100 F (rectal); pulse, 88 per minute and regular; respirations, normal at rest. The skin and mucous membranes were pale. There was enlargement of the postauricular, submandibular, supraclavicular, axillary, epitrochlear, inguinal, and medial malleolar lymph nodes. Pain and tenderness were present over the maxillary sinuses, and darkness of each antrum was noted on transillumination. The nasal airway was completely obstructed by a fetid, profuse, sanguinopurulent discharge. After cleansing, thick creamy pus came from each middle meatus. A granulomatous overgrowth involved the anterior portion of the nasal septum and middle turbinates. These areas were friable and bled easily. There was complete anosmia. Purulent fluid was present in each middle ear. The ophthalmologic examination, including visual fields, was normal; visual acuity was 20/20. The lungs were clear. There was a systolic murmur at the apex, not transmitted. Neurological findings included anesthesia of the upper eyelids, nose, and malar eminences and an equivocal right foot drop. The remainder of the physical examination was within normal limits.

Summary of Admission Laboratory Findings.—There was 1+ to 4+ albuminuria and microscopic hematuria; occasional hyaline and granular casts were found. The specific gravity of the urine was 1.021. The blood NPN was 27 mg. %. The serologic Kahn test was negative. The hemoglobin was 6.4 gm. %; RBC, 3,600,000; the red blood cell indices were compatible with a blood-loss anemia; sedimentation rate, 22 mm. per hour (cor.); WBC, 9,400, with a normal differential count; there were adequate platelets, and hypochromic, microcytic red blood cells. Sternal marrow examination revealed normoblastic erythrocytic hyperplasia compatible with a blood-loss anemia. Bleeding and clotting times and clot retraction were normal. Complement-fixation and skin tests were negative for histoplasmosis, blastomycosis, and coccidioidomycosis, as were skin tests for lymphogranuloma venereum and tuberculosis (OT, 1:10,000). A complement-fixation test for glanders disease was not done. Specimens of the nasal discharge showed Gram-positive cocci, coagulase-positive staphylococci, but no fungi or AFB. Gastric washings were likewise negative for AFB. Inoculations of nasal biopsy material into mice and chick embryos revealed no viral or tuberculous organisms. The thyroid and gonad studies were normal: BMR, +2; serum cholesterol, 264 mg. %; 24-hour I^{131} uptake, 26%; PBI, 5.3μg. %; FSH assay (urine) 3 M.U. per 24 hours.

X-ray examinations revealed a chronic pansinusitis with evidence of bone destruction and a solitary nodular "snowball" density in the left lower lung field, 7 cm. in diameter (Figs. 12 and 14).

Biopsy specimens from the nose showed vascular pyogenic granulation tissue, with giant cells of the foreign-body type, numerous eosinophils, and intimal fibrinoid necrosis of the blood vessels.

Course.—During the first two weeks of hospitalization the patient was bedridden and complained of severe, dull pain about the upper teeth and maxillae. He developed a cellulitis over the right maxillary antrum and lower eyelid, with temperature elevations to 102.4 F (rectal) and without leukocytosis. Antibiotics did not materially influence the facial inflammatory reaction. Transfusions of whole blood, to a total of 3,000 cc., brought the hemoglobin from 6.4 to 12 gm. % and completely relieved the symptoms due to blood-loss anemia.

On the 15th day (Jan. 2, 1954) corticotropin therapy was started. He was given repository corticotropin injection, 60 mg. (clinical units) q. 12 hr., I.M., daily; a diet of 800 mg. sodium restriction, and 6 gm. KCl daily. Twenty-four-hour urine specimens for 17-ketosteroids and 17-hydroxycorticosteroids were run prior to therapy and repeated at regular three- to four-day intervals to verify optimal adrenocortical effect (Table 14). Fasting blood sugar determination, glucose-tolerance test, and eosinophil counts were also done. The course in the hospital with onset of corticotropin therapy was very dramatic. The temperature returned to normal; the epistaxes stopped; the facial cellulitis disappeared, and the patient was up and about without complaints except for occasional migratory arthralgia.

On the 21st hospital day a large septal perforation involving the quadrangular cartilage and perpendicular plate of the ethmoid was noted, as was a gradually developing saddle-nose deformity (Fig. 2). The lung lesion had decreased in size and density. The daily corticotropin dosage was gradually reduced to 40 units, and the patient was discharged on the 41st hospital day (Jan. 26, 1954) on 40 units of repository corticotropin injection and steroid adjuvant therapy, to be followed as an outpatient at monthly intervals.

After one month of relatively good health, the patient suffered an exacerbation in March, 1954. While at home, he developed moderate facial pain, ptosis, and decreased vision in the left eye. The patient was readmitted on March 9, 1954. Physical examination showed paralysis of cranial nerves III and VI, and proptosis with amaurosis, O.S.; a severe saddle-nose deformity; moon facies; acneform rash of the face, neck, and trunk; buffalo hump, and muscle wasting. A considerable mass of foul-smelling crusts filled the nasal cavity. When the nose was cleansed there was found to be a single cavity separated only by the anterior and posterior columellae. The bony turbinates were exposed bilaterally. Chest x-ray showed a decrease in size of the lesion in the left lower lobe to 3.5 cm. but also revealed a new mottled density in the right lower lobe. The patient was very depressed over the loss of vision in the left eye.

In May, 1954, there was impairment of ocular muscle movements and of visual acuity in the right eye. The clinical impression was that of granulomatous invasion into the orbits and base of the brain. Surgical decompression of the right orbit was considered to prevent further visual loss, but the operation was not performed in view of the rapid progression of the granulomatous-destructive process following surgical procedures in the advanced stage of this disease attested by a review of the patients described in the literature.

A progressive downhill course was noted in spite of corticotropin therapy. There was development of right ptosis, proptosis, and complete blindness; generalized weakness, and intractable facial pain. The patient was readmitted on Sept. 13, 1954, at which time he received narcotics, sedatives, corticotropin, cortisone, PABA, and mechlorethamine hydrochloride (nitrogen mustard) therapy. Examination of the nose revealed a common nasal chamber separated only by the anterior membranocutaneous columella. The turbinate structures of the nose were absent (Figs. 10 and 19). The medial wall of the maxillary antra appeared devoid of bone. Only thickened mucous membrane separated these sinuses from the nasal cavity. The patient was transferred to the medical service of the Veterans Administration Hospital, Ann Arbor, where he died of "apparent complete exhaustion," on Dec. 1, 1954, forty-three months after onset of illness.

The clinical diagnoses were (1) Wegener's granulomatosis and (2) Cushing's syndrome. The anatomic diagnoses were (1) severe chronic granulomatous inflammation of the nares, nasal sinuses, dura, left orbit, and left lung; (2) chronic healed focal glomerulitis (Wegener's granulomatosis), and (3) Cushing's syndrome (corticotropin and cortisone therapy).

Case 122.—A 50-year-old housewife was admitted to University Hospital on Sept. 10, 1953, with the complaint of "marked deafness and blood with pus from the nose." Approximately 19 years previously (1934) the patient noted gradual onset of bilateral nasal obstruction and mucoid nasal discharge. The family physician took nasal cultures and made an autovaccine with which the patient was inoculated but without results. Nasal irrigations and antiseptic instillations did not alleviate the symptoms. In 1944 the family physician made a diagnosis of "sinus trouble with polyps and adhesions in the nose." In 1948 the nasal obstruction and discharge ceased spontaneously and the patient was able to breathe through the nose for the first time in 14 years. She was asymptomatic until October, 1952 (four years) when she developed a "cold" characterized by profuse purulent nasal discharge. The family physician treated the patient with penicillin; "after a few shots she broke out into hives." The purulent nasal discharge continued. In February, 1953, there was onset of migratory joint pains which involved the knees, wrists, shoulders, ankles, and fingers with associated arm and calf pain and soreness, tenderness, redness, heat, and swelling of the involved joints. A diagnosis of "rheumatism" was made, and the patient was treated with corticotropin and cortisone (dosage not known) for two months. In April, 1953, the nasal discharge became more profuse with pain about the nose and face. A local physician "removed polyps from each side of the nose and bone structures." In May, 1953, the nasal discharge was foul smelling and blood-streaked. Similar foul-smelling material drained from the right ear with progressive deafness. The patient was hospitalized for 3 weeks for "pneumonia and a collapsed lung resulting from the nasal operation." In July, 1953, the patient had severe pain in the nose, radiating into the teeth and maxillary sinuses. Hearing acuity in the right ear was almost gone. She received x-ray treatments to the nose which partially relieved the pain but did not influence the profuse, purulent, fetid character of the nasal discharge. In August, 1953, there were anorexia, weakness, night sweats, and a 15 lb. weight loss. Chest x-ray on Aug. 8, 1953, was normal. Bilateral myringotomies for suppurative otitis media,

A.U., revealed a copious quantity of fetid, purulent discharge. The patient was placed on streptomycin therapy, 0.5 gm. b.i.d. for 13 days. The patient became virtually deafened prior to admission to University Hospital. There was no history of atopic allergy. During the preceding 25 years the patient had made frequent trips to Arkansas, Texas, and Florida. The patient had noted abrupt cessation of menstrual periods in May, 1953.

Physical Examination.—Blood pressure 140/100 (R.A.R.); temperature, 98.6 F (rectal); pulse, 96 per minute and regular; respirations, 16 per minute. The patient was a well-developed, well-nourished, acutely and chronically ill white woman, who appeared older than her stated age. She was in pain and very depressed; a very fetid odor was present at the bedside. The skin and mucous membranes were of normal color. There was no palpable lymphadenopathy. Tenderness was present over the maxillary sinuses, and darkness was noted on transillumination. The ophthalmologic examination was normal. The nasal airway was obstructed by a profuse fetid discharge, which was purulent and bloody. After the nose and nasopharynx were cleaned, a fiery-red, ulcerated, granulomatous process was seen to involve the septum and floor of each nasal fossa. There was a 0.5 cm. anterior septal perforation with ulceration of the right inferior turbinate. The mucosa of the nasopharynx was edematous and granulomatous. Bloody pus was present in each Eustachian tube orifice. The mouth, oropharynx, and larynx were not involved. The ears showed bulging of each tympanic membrane, with obliteration of all the landmarks. The patient was very deaf; she could only hear a loud shout at the bedside and utilized lipreading with difficulty. The lungs were clear. The remainder of the physical examination was within normal limits.

Laboratory Data.—Urine: (catheter specimen) trace of albumin, microscopic hematuria, and occasional hyaline, granular, and waxy casts were found. Specific gravity was 1.010. Bence Jones test was negative. Blood: Kahn test was negative. NPN was 29 mg. %. Hemoglobin was 10.5 gm. %; RBC, 4,300,000; hematocrit, 27%; M.C.V., 88 cu.μ; M.C.H.C., 27.6%; sedimentation rate, 31 mm. per hour (cor.); WBC were 10,000, with 1 band neutrophil, 78 segmented neutrophils, 9 lymphocytes, 8 monocytes, 3 eosinophils, and 1 basophil; the red cells were uniform; platelets were increased. Total serum proteins were 8.5 gm. %, with albumin of 3.4 and globulin of 5.1; A/G ratio was 0.7. L.E.-cell test was negative. Complement-fixation test and skin tests were negative for histoplasmosis, blastomycosis, and coccidioidomycosis, as were skin tests for lymphogranuloma venereum and tuberculosis (OT, 1:10,000). The complement-fixation test for glanders was negative. Specimens of the nasal discharge showed few γ-hemolytic streptococci and many hemolytic coagulase-positive staphylococci, but no fungi or tubercle bacilli were found. Blood cultures were negative. Gastric washings were also negative for AFB. Inoculation of nasal biopsy material into mice and chick embryos revealed no viral or tuberculous organisms. Paranasal sinus x-rays revealed a pansinusitis with thickening of mucous membrane and clouding. Bone destruction was evident by partial absence of turbinate structure. The nasal passages were filled with a homogeneous soft tissue density (Fig. 9). Chest x-rays revealed a 3 cm. nodular density in the left upper lung field and a smaller 1 cm. nodule in the right lower lobe (Fig. 11). Biopsy specimens from the nose revealed severe purulent necrotizing granulomatous reaction with Langhan's type giant cells. There was no evidence of specific infective granuloma or malignancy.

Course.—Bilateral myringotomies were performed on admission, with release of a copious amount of fetid pus. Bacteriologic studies were similar to the organisms obtained from the nasal discharge. The hearing was not improved, however. The ears continued to drain and were cleansed b.i.d. with saline irrigations and boric acid-alcohol drops. The patient was given erythromycin as per antibiotic sensitivity studies on organisms found in nasal and aural discharge, without any influence on the course of the disease. A smear of the nasal discharge taken by the dermatology consultant, along with the appearance of the granulomatous tissue in the nose and the unremitting course of the disease, was thought to be compatible with rhinosporidiosis (Rhinosporidium seebri), but culture on chick embryos, as well as histologic examination of biopsy material, failed to substantiate this diagnosis. The therapy offered was pantavalent antimony in the form of stilbamidine, which also did not alter the course of the clinical picture. The possibility of pulmonary metastatic carcinoma from the gastrointestinal and genitourinary tracts was considered. However, clinical and roentgenographic studies failed to substantiate this impression.

By the 42d hospital day the patient's condition had deteriorated. She had severe facial pain which required round-the-clock narcotics. The septal perforation increased in size, and the nose began to saddle. The episodes of acute migratory arthritis and bursitis were severe and without response to salicylates and antibiotics. X-rays of the chest revealed that the nodular density in the left upper lung field increased in size and began to excavate, with central cavity formation but without any signs or symptoms referable to the lungs (Fig. 11). Multiple cutaneous granulomata appeared on the buttocks and deltoid sites of intramuscular

injections. The anorexia and weakness were severe, and the patient required frequent intravenous supplements. The hemoglobin fell to 8.8 gm. %, but blood transfusions did not noticeably affect the course of the disease. The white blood cell count varied from 9,000 to 14,000, with a shift to the left. Microscopic hematuria, albuminuria, and cylindruria had become more pronounced, but the NPN did not rise. The patient appeared completely exhausted, slept most of the day, and was becoming moribund.

On the 48th hospital day (Oct. 28, 1953) corticotropin was started. She was given repository corticotropin injection, 100 clinical units I.M. daily, a diet of 800 mg. sodium restriction, and 6 gm. of KCl daily. Twenty-four-hour urine specimens for 17-ketosteroids and 17-hydroxycorticosteroids were run prior to therapy and repeated at regular three- to four-day intervals to verify optimal adrenocortical effect (Table 14). Fasting blood sugar test and eosinophil counts were also done. The response to corticotropin therapy was dramatic! On the third day of corticotropin therapy the patient was ambulatory. The arthralgia and bursitis had disappeared. The nasal discharge decreased, and the nasal airway opened up. The ears stopped draining. The tympanic membranes were intact, and the landmarks were becoming visible. The appetite improved. The patient was very euphoric. Subsequently, she could hear. The pulmonary masses decreased in size. The menstrual periods returned. The urinalysis became normal. The dose of corticotropin was gradually reduced, and the patient was discharged on the 66th hospital day, Nov. 14, 1953, on 40 units of repository corticotropin injection and steroid adjuvant therapy, to be followed at monthly intervals by the otolaryngology and endocrine and metabolism clinics.

While at home, her hearing continued to improve. The tympanic membranes were thickened, but the landmarks were visible. An air-conduction hearing aid was prescribed for the right ear, with good results. The nose was irrigated with saline daily, sometimes with removal of large chunks of necrotic tissue. The saddle nose deformity became more pronounced. There was a 2 cm. perforation in the nasal septum, involving the quadrangular cartilage and perpendicular plate of the ethmoid. The turbinates were atrophic. There were minimal granulomations on each side of the septum at the periphery of the perforation. The remainder of the nasal mucosa had a healthy appearance. The chest x-ray showed decrease in the size of the pulmonary nodules. The patient felt sufficiently well to do house chores and vacationed in Florida for four weeks. The dose of corticotropin was gradually decreased to 10 units daily because of excessive adrenocortical function. With this dosage reduction, there was increased fatigue and increased nasal obstruction with facial pain.

On March 5, 1954, the patient was readmitted because of hoarseness, stridor, and dyspnea. Physical examination revealed a diffuse papilliferous granulomatous involvement of each vocal cord with subglottic extension. The corticotropin dosage was increased to 40 units b.i.d., and within 36 hours the vocal cords assumed their normal appearance. On the third hospital day the patient was discharged on 40 units of corticotropin daily, to be followed at two-week intervals.

During March, 1954, at home, the patient noted facial discomfort, which was described as deep bone pain and localized to the middle of the palate. The patient developed difficulty with equilibrium, which was described as postural and positional unsteadiness rather than true vertigo. Symptoms of endocrine dysfunction began to reappear. There were 10- to 15-minute episodes of sheer exhaustion upon doing a little work, such as washing dishes. The patient had developed moon facies. The dry, scaly character of the skin, along with thinning of the eyebrows, was suggestive of hypothyroidism. The patient was placed empirically on 1½ grains (0.1 gm.) of desiccated thyroid per day and the daily administration of 40 units of corticotropin was continued.

On April 1, 1954, the patient was admitted to University Hospital for the third time, with complaints of decreased vision, facial pain, and return of hoarseness. Physical examination revealed that the patient had developed hypertension, 180/120 (R.A.R.), a moon face and bison type cervical curvature, features associated with excessive adrenocortical activity (Fig. 19*C*). The ophthalmologic examination revealed a proptosis and ptosis of the left eye. There was slight myopia, with difficulty in convergence and focusing on close objects. The dorsal support of the nose caudal to the nasal bones was absent, forming a complete saddle. The nasal interior was a single cavity separated by the anterior and posterior columellae. The fetid odor had returned after a four-month period. A granulomatous process involved the inferior and middle turbinates with copious purulent discharge coming from each middle meatus. Mirror laryngoscopy revealed a subglottic granuloma, which partially compromised the airway. The remainder of the physical examination was within normal limits except for a diffuse tendon hyperreflexia. Laboratory data revealed a return of albuminuria (1+) but the blood NPN was normal (40 mg. %). A leukocytosis of 19,400, with a shift to the left, was probably a reflection of long-term steroid therapy. Paranasal sinus films showed marked loss of turbinate and nasal septum detail indicative of advanced bone destruction.

The laryngeal granuloma responded to steroid and antibiotic therapy. The patient was discharged on the seventh hospital day.

At home the patient felt stronger and she was able to resume her household duties. She was very concerned with the progressive loss of vision. It was felt that surgical intervention to prevent visual loss was not indicated in view of the rapid progression of the granulomatous destructive process following operative procedures in the advanced stage of this peculiar disease. The therapeutic plan was to sustain a progressive and florid Cushing's syndrome, if necessary, in an attempt to keep down the necrotizing granuloma that was involving the eyes. Although some of the ominous sequelae of chronic steroid administration were neutralized by specific prophylactic measures testosterone (cyclopentylpropionate, potassium, and a low-sodium diet), other manifestations of excessive corticoid activity inevitably appeared. Thus, she developed a Cushing's type central obesity with tubular arms and legs, pronounced moon facies (Fig. 19*C*) and a buffalo hump. The blood pressure ranged between 180/120 and 150/85 (R.A.R.).

In October, 1954, the patient suddenly developed abdominal cramps, hematemesis, and melena. She was readmitted (fourth admission), and a profound prolapse of the gastric mucosa and a duodenal ulcer were found on roentgen examination. The surgical consultant advised conservative therapy, and the patient made a good recovery. The daily steroid therapy at this time was 40 units of repository corticotropin injection and 50 mg. of cortisone (Compound E), both intramuscularly.

In December, 1954, the failing vision progressed. Visual acuity in the right eye was 20/200, and there was only light perception in the left eye. Paranasal sinus x-rays showed erosion of the walls of the sphenoid sinuses. The facial pain was only minimal; the single nasal cavity showed complete absence of turbinate structures, but the mucosa was healthy. In March, 1955, the patient had become addicted to meperidine (Demerol). In March, 1955, the steroid therapy was changed to prednisone (Meticorten), 25 mg., p.o. daily in divided doses. There was considerable reduction in the hyperadrenal habitus (Fig. 19*D*), and the blood pressure returned to normal. Chlorpromazine and phenobarbital were given to reduce the insomnia and the hyperirritability associated with hyperadrenalism. In May, 1955, there was complete blindness, primary optic atrophy, O.U., and heavy meperidine addiction. Episodes of cutaneous granulomata over the deltoid and the buttock injection sites responded to antibiotic therapy and increased steroid dosage.

In January, 1956, the chest x-ray showed complete resolution of the nodular pulmonary lesions observed prior to steroid therapy, except for a small subpleural linear scar (Fig. 18). From January, 1956, until April, 1957, sixteen months, there was no clinical evidence of active granulomatous disease. The urinalysis was consistently negative for albuminuria and cylindruria. The blood pressure did not rise above 150/100 (R.A.R.) during follow-up examinations. There were occasional upper respiratory infections, with poor host resistance, which required hospitalization and antibiotic therapy. The patient became allergic to oxytetracycline (Terramycin), tetracycline (Achromycin), and codeine phosphate.

In April, 1957, the patient was admitted for the 12th time because of deep substernal pain associated with nausea and a general ill feeling without being able to be more specific. The upper and lower respiratory tract showed no clinical evidence of active granulomatous disease. On the fifth hospital day, April 19, 1957, the patient died suddenly of a myocardial rupture secondary to myocardial infarction with acute cardiac tamponade—approximately four years after onset of active disease. The ECG was normal 48 hours prior to death. A complete postmortem examination including temporal bones and ocular tissues was performed.

Pathological Diagnosis. — Myocardial infarct with cardiac rupture and cardiac tamponade. Coronary atherosclerosis. Wegener's necrotizing granulomatosis of midline facial tissues with active disease in nasopharynx, sphenoid sinuses, and maxillary sinuses. Destruction of nasal septum and turbinates. Old perforation in roof of right sphenoid sinus. Old focal pachymeningitis of anterior cranial fossa. Amaurosis. Primary optic atrophy with retrograde degeneration of nerve fiber layer and ganglion-cell layer of the retina. Focal subpleural fibrosis without evidence of pulmonary granulomata. Anterior pituitary basophilism. Moderate adrenocortical atrophy. Nodular thyroid gland with follicular adenoma. Marked degenerative fatty atrophy of the liver; atrophy of endometrium and ovaries. Marked arteriosclerosis of kidney. Osteoporosis.

CASE 123.—A 52-year-old white factory inspector was admitted to University Hospital on Jan. 22, 1957, with the complaint of continuous sore throat. The patient was in good health until June, 1956, when he noted sudden onset of pharyngeal pain. The family physician prescribed penicillin without relief. After penicillin was stopped, the patient developed ulceration of the palate, pharynx, and larynx, for which he was hospitalized for eight weeks and treated with "every available antibiotic" without effect. There was an associated bronchopneumonia with temperature spikes to 102 F. A granulomatous lesion of the epiglottis was biopsied and showed a nonspecific granuloma. The

lesions appeared to heal of their own accord. In November, 1956, the patient developed purulent nasal discharge without pain and swelling over the left maxillary sinus. A Caldwell-Luc operation was performed, and moderate suppuration was found. The left middle turbinate was removed because it was gangrenous. The operative site healed well. In January, 1957, the patient developed a right-sided sore throat, which persisted, and he was referred to the University Hospital. There was a history of low back pain and limitation of motion at the hips because of degenerative arthritis since 1953.

Physical examination revealed a well-developed, well-nourished white man, who appeared somewhat chronically ill. The blood pressure was 135/85 (R.A.R.); temperature, 98.6 F (oral); pulse, 80 per minute and regular; respirations, 18 per minute. There were no palpable lymph nodes. The nose was filled with crusts. There was a fetid purulent discharge from the left nasal chamber. A patent nasal-antral window was present on the left side. The edges of the window were covered by friable granulation tissue anteriorly. The left middle turbinate was surgically absent. There was partial destruction of the vomer at the posteroinferior portion of the nasal septum, with bone denuded of mucous membrane. The nasopharynx was diffusely hyperemic. The right tonsil was twice the size of the left and was covered by tenacious purulent exudate, which when removed revealed an ulcerogranulomatous process. There was diffuse peritonsillar hyperemia. There was an arthrokatadysis (Otto's pelvis) of both hips with limitation of motion.

Laboratory Data.—The urinalysis was within normal limits. The Kahn test was negative. The NPN was 38 mg. %; fasting blood sugar was 90 mg. %. The hemoglobin was 12.3 gm. %, with normal red cell indices. The sedimentation rate was 44 mm. per hour (cor.). The WBC were 6,900, with a normal differential. Complement-fixation tests and skin tests for histoplasmosis, coccidioidomycosis, and blastomycosis were negative. The tuberculin test (OT, 1:10,000) was negative, as was the complement-fixation test for glanders. The L.E.-cell test was negative. Specimens of right tonsil exudate showed Neisseria catarrhalis, a viridans streptococcus, Hemophilus hemolyticus, and diphtheroids. There were many Gram-positive cocci in the material taken from the nose. Paranasal sinus x-rays revealed destruction of the inferoposterior portion of the nasal septum and diffuse clouding of the left maxillary sinus and ethmoidal labyrinth. The chest x-ray was normal. Various biopsy specimens from the nose and larynx (outside slides included) revealed "changes consistent with so-called lethal midline granuloma." A calf muscle biopsy showed no vasculitis or myositis.

During the first 10 hospital days there were frequent temperature elevations between 100 and 101 F (rectal), with associated episodes of diffuse diaphoresis. Blood cultures taken during these episodes were negative. There were anorexia, weakness, and a feeling of listlessness. On the 11th hospital day the patient was started on oral hydrocortisone, 200 mg. in four daily divided doses; 800 mg. sodium diet, and 6 gm. of KCl daily. The clinical improvement was rapid. The tonsillar granuloma began to heal; the nasal discharge diminished, and the nasal airway once again became patent. The dose of hydrocortisone was reduced over a 10-day period to 80 mg. daily. On the 21st hospital day, 40 mg. of prednisone in four divided doses was substituted. This also was gradually reduced to 30 mg. daily. The patient was discharged on Feb. 26, 1957, the 36th hospital day, on 20 mg. of prednisone daily. He was to be followed at monthly intervals.

In March, 1957, the tonsillar granuloma had healed completely. The nasal granulomatous process appeared less active, even though there was a 1 cm. perforation in the vomer and perpendicular plate of the ethmoid. It was felt that the lesion was "demarcating." The 20 mg. daily dose of prednisone was continued. There were no manifestations of excessive corticoid activity.

In April, 1957, the patient developed ankle and shoulder arthralgia, with reactivation of the low back pain and limitation of hip motion. The patient was readmitted in May, 1957, on the orthopedic service, for consideration of a Vitallium cup arthroplasty for correction of Otto's pelvis. However, the operation was deferred in view of the previously observed systemic spread and rapid progression of the granulomatous destructive process in the advanced stage of this disease. The patient was not satisfied and left the hospital to seek a "curing operation for the hip condition." The granulomatous lesion in the tonsil remained healed; there was a septal perforation, but the nasal mucosa was beginning to look normal again. The chest x-ray was negative. The patient was not seen again.

In June, 1957, a cup arthroplasty of the left hip was performed elsewhere. Adrenal cortical steroid therapy was continued by the local physician. The postoperative course was stormy and downhill. The nasal granuloma progressed, with exteriorizing necrosis of the left side of the nose and cheek. Pneumonitis and lung abscess developed. The patient died on Sept. 29, 1957—approximately 16 months after onset of illness. No postmortem examination was performed.

CASE 124.—A 52-year-old housewife visited the University Hospital on April 24, 1945, for evalua-

tion of a nasal alar deformity and bloody, purulent nasal discharge. The patient had right-sided nasal obstruction with crust formation for approximately five years. In March, 1944, she experienced gradual onset of a persistent, purulent nasal discharge with increased crust formation. A local physician "scraped the crusts" with temporary relief, but after several "treatments" the patient developed epistaxis and the nasal discharge became more profuse and musty in odor. In December, 1944, the patient noted ulceration with "thick brownish-black crusts" on the mesial aspect of the right nasal ala and within the nasal vestibule. There was no relief of symptoms by antiseptic instillations, irrigations, or systemic antibiotics. Gradually, contracture of the alar skin was noted with an obvious cosmetic deformity. The family history was significant in that the patient's father died of pulmonary tuberculosis, but there was no history of direct exposure.

Examination on April 24, 1945, revealed that the right nasal ala was pulled upward. Inside the nasal vestibule there was some firm, slightly bleeding granulation and scar tissue, which extended upward to involve the inner aspect of the lateral crus of the lower lateral cartilage. There was a contracture deformity of the right external naris. The clinical impression was a chronic infectious granuloma, possibly lupus vulgaris. Biopsy of the area showed vascular granulation tissue without evidence of specific infective granuloma. The serologic Kahn test was negative.

The lesion in the nasal vestibule gradually healed. Except for nasal crusting, the patient did not complain until September, 1947, when she noticed a "hole in the inside of the nose." Examination at University Hospital on Dec. 22, 1947, revealed the above-described alar deformity with scar tissue in the nasal vestibule. There was a 1×1 cm. perforation of the nasal septum. The septum was thickened and granulomatous. Involvement appeared as the same type of necrotizing granulomatous lesion that was previously seen in the nasal vestibule. The right inferior and middle turbinates, the left side of the nasal septum, and the floor of the left nasal chamber were also involved. The patient was admitted for further evaluation and treatment on Jan. 20, 1948.

Physical examination revealed a small-statured, well-nourished white woman who did not appear acutely or chronically ill. The blood pressure was 115/75 (R.A.R.); temperature, 99 F (oral); pulse, 80 per minute and regular; respirations, 18 per minute. The skin and mucous membranes were of normal color. There was no palpable lymphadenopathy. Except for the previously described lesions in the nose, the physical examination was within normal limits.

Laboratory Data.—Findings on urinalysis were normal. Blood: The Kahn test was negative. The hemoglobin was 12.5 gm. %, with normal red cell indices. The sedimentation rate was 20 mm. per hour (cor.). WBC were 5,000, with a normal differential. Skin tests for blastomycosis, histoplasmosis, and coccidioidomycosis were negative. The tuberculin test (OT, 1:10,000) was weakly positive. Specimens of nasal discharge showed Gram-positive cocci and diphtheroids. No fungi or AFB were found. Paranasal sinus x-rays revealed clouding and mucous membrane thickening of the right maxillary antrum, with bone destruction involving the nasal septum and right inferior and middle turbinates. The chest x-ray was normal.

Hospital Course.—On Jan. 26, 1948, the patient was taken to the operating room. The nasal septum was extensively removed in full thickness back to the rostrum of the sphenoid and to the posterior columella. The right middle turbinate was amputated. Granulomatous mucous membrane in the middle meatus was also removed, and some of the ethmoid cells were entered. There was remarkable avascularity throughout the operation, suggesting the possibility that the lesion was an obliterative endarteritis. Histologic examination showed active, chronic suppurative osteomyelitis, with overlying pyogenic granuloma. No malignancy. No evidence of specific infective granuloma. The postoperative course was uneventful, and the patient was discharged on Jan. 30, 1948.

The nasal discharge and crusting continued, though diminished. In September, 1948, the granulomatous process involved the left side of the nose. In April, 1949, the purulent nasal discharge and crusting became profuse and somewhat fetid. On Sept. 2, 1949, the patient was again hospitalized and the left inferior and middle turbinates were amputated. There was very little bleeding. Healthy tissue was reached upon removal. No nasal packing was required postoperatively. In January, 1950, the nose was a common chamber but in excellent condition with very little crusting (Fig. 4). In April, 1954, a plastic operation to release the scar from the right nasal ala was performed elsewhere. The patient is well to date except for nasal crusting, which can be flushed from the nose with saline irrigations—12 years after onset of active disease. A subsequent review of the histological material shows that this disease process is "compatible with so-called lethal midline granuloma."

Anesthetics and Premedication in Peroral Endoscopy

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When a patient is seen and endoscopy is indicated, his psychic preparation is very important. The patient should know a great deal about what we are planning to do so that we may have full cooperation. We must tell the patient that this is an examination and not an operation, and that there will be no pain but probably some discomfort because his neck will have to be extended and kept in this position for a little while. He must know that he will not be able to talk during the procedure because the tube is in his voice box, but that he will have all the air he needs for respiration at all times, and that, because we are using a rigid tube, any jerky movements might be dangerous. Having prepared the patient in this manner, the next important step is the medical preparation.

In order to have an ideal patient on the operating room table, we have to aim for (1) a relaxed patient, without fear, who is unconscious, (2) a sleeping but arousable patient, (3) diminished or absent laryngeal and bronchial reflexes, (4) diminished secretions, (5) little or no depression on the respiratory or circulatory centers, (6) an active cough reflex postoperatively, (7) partial or complete postoperative amnesia, and (8) anticipation of possible toxic reactions from any topical anesthetic used.

General or topical anesthesia can be used for endoscopies. The *indications* for *general anesthesia* are present in the following instances.

1. The patient has a difficult anatomy, such as excessive fat, a short neck, large tongue, narrow mandible, infantile epiglottis, and immovable false or fragile teeth.

2. The patient is apprehensive and expresses the wish to have general anesthesia.

3. The patient has a cardiovascular disease, and we do not like to put him under any unnecessary stress. We feel that, even though the procedure is explained to him he will be somewhat apprehensive about a bad heart, but that he will have almost no worry if he is told that he will be asleep during the procedure.

4. The performance of suspension laryngoscopy or fuller direct inspection probably is not obtainable unless the patient is fully relaxed.

The *objections* to *general anesthesia* are as follows.

1. It may be considered a bigger procedure.

2. The hazard is increased in a few patients (e.g., in children with acute respiratory obstruction) and in the presence of foreign bodies or vascular anomaly.

3. In emergencies there is no time for general anesthesia.

4. Greater personnel is required for the procedure.

The *general anesthetics* now being used are as follows.

1. Ether may be given by inhalation or rectally. The disadvantages of inhaled ether are (*a*) a shimmering effect or mirage in the visual field which inhibits good examination (especially in children) through small lumen bronchoscopes; (*b*) the ever-present danger of explosion from any electrical equipment; (*c*) the postoperative nausea, possible vomiting, and remote, but always possible, vomitus aspiration, and (*d*) the reduced or absent cough reflex, postoperatively, for a prolonged period.

2. Tribromoethanol (Avertin) anesthesia may be administered rectally, usually in children. The disadvantage here is, once given, it cannot be reduced.

3. Thiopental (Pentothal) can be given intravenously with barbiturate, opiate, and atropine as premedications to perform an easier endoscopy. Thiopental has proven to be a cause of occasional severe laryngeal spasm, but this can almost always be readily circumvented.

4. Curare may be added to the intravenous thiopental and oxygen insufflation via the

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bronchoscope or endotracheal tube if esophagoscopy becomes necessary.

5. The thiopental and curare general anesthesia technique has been further developed by the use of manual artificial respiration or a respiration-bronchoscope through which intermittent positive pressure can be applied.

The techniques mentioned in items 3 to 5 limit the time for endoscopy from five to ten minutes because the patients become cyanotic or anoxic in a very short time, and even manual respiration and oxygen insufflation before and during the procedure do not permit maintaining the patient this way for a longer period without possible damage to the brain.

In an effort to improve the technique, we developed, at the Long Island College Hospital, a safe method of general anesthesia with passive respiration which gives the endoscopist all the time he needs for examination or surgery. In this method we use thiopental (Pentothal) and succinylcholine, with an artificial respirator (portable polio type) which produces an exchange of from 300 to 1,000 cc. of air or oxygen. This, in many cases, is even more than the exchange of the patient before endoscopy and has an advantage in performing bronchoscopy on patients with chronic pulmonary disease and reduced vital capacity. However, hyperventilation in the conscious produces undesirable effects and should not be indulged in during this controlled procedure.

Premedication.—The usual routine premedication for endoscopies is a combination of (*a*) barbiturate, (*b*) opiate, and (*c*) hyoscyamine. (*a*) Pentobarbital (Nembutal) acts quickly, 100 to 200 mg., one hour prior to endoscopy; (*b*) meperidine (Demerol), 50 to 100 mg.; (*c*) atropine, 0.32 to 0.4 mg. Both meperidine and atropine are given 45 minutes prior to endoscopy. On children, barbiturate is given on the basis of age; meperidine and atropine on the basis of weight. To asthmatics, only a barbiturate is given. Some clinics add epinephrine to the topical anesthesia but the majority of endoscopists feel that epinephrine mixed with the topical anesthetic might favor arrhythmia and fibrillation of the heart; if it is given, it should be given by hypodermic only. The barbiturate is given to counteract any toxic effect from the topical anesthetic which is going to be used. Therefore, it should be given at a time that meets the time of maximum effect of the topical anesthetic, which is about 20 minutes after application.

In order to meet all previously mentioned eight requirements for an ideal patient, we suggest for use what is called potentiated anesthesia, developed in Europe and now adopted in the United States. We say potentiated anesthesia if we use phenothiazines in combination with meperidine and hyoscyamine, atropine or scopolamine, in our premedication. Carpentier (France) first synthesized, in 1950, phenothiazines, and Laborit (France), in 1951, first used chlorpromazine (Thorazine) in anesthesia.

A few words about the pharmacology of chlorpromazine. Its action protects against stress phenomena by altering the ability of the organism to respond to external aggression. One might say the body is in transition toward hibernation or in a stage of hypometabolism. Chlorpromazine acts centrally as a unique depressive on the reticular activating system (R.A.S.) of the brain stem, the hypothalamus, and the autonomic nervous system as well as peripherally by decreasing the reflex irritability of the pharynx, larynx, ond bronchi. The emotional corticofugal projections are also interrupted in the R.A.S., which brings the patient into a state of emotional indifference, or, pharmacologically, into a state of pharmacodynamical frontal lobotomy. The muscle tone and reflex activity located in the same area of the brain stem are decreased by chlorpromazine, leading to a muscle tone weakness. The respiration is deep and regular. The need for oxygen is decreased because the metabolism is lowered, so that one does not have to worry about a low respiration rate as long as it is deep and regular. The patient is also asleep but easily awakened and responsive to

commands. Side effects of chlorpromazine are very few. The most important one, perhaps, is a slight decrease of the blood pressure, which is not marked if the patient is kept in supine position and is not allowed to sit or stand up.

During the first few endoscopies performed with this kind of premedication, decrease of blood pressure of about 10 to 30 mm. Hg was found, and one patient with hypotension came close to syncope when he sat up for topical anesthesia application. Likewise, it was found that the amount of anesthetic needed for good topical anesthesia was much less than usually needed, and the technique of application of the topical anesthetic was changed. The patient does not sit up as usual but is kept in a supine position on his stretcher and is not moved onto an operating room table. All attachments, such as a head holder for positioning, can be put on the stretcher, the wheels of which are lockable. A slotted (Magil or Foregger type) laryngoscope, such as the anesthetist uses for endotracheal intubation, is used to expose the base of the tongue and hypopharynx, which is sprayed a couple of times. Then the epiglottis is lifted up and, with a laryngeal cannula, about 1 cc. of topical anesthetic is applied into the larynx and trachea. Soon the bronchoscope can be introduced with ease, and further anesthesia, a few drops into the right and left main bronchus, or a spray applied through the bronchoscope, can be administered. Because of reduced bronchial reflex, the cough which usually would have been violent is mild and slight, so that the bronchoscope can be left in the trachea without any objection until anesthesia of the bronchial mucosa is effective. Right after the bronchoscopy, about 90% of all patients have a very strong cough, which meets a condition of ideal procedure.

Promethazine (Phenergan), another phenothiazine, is a potent antihistamine with prolonged action. Otherwise, its action is similar to that of chlorpromazine. It is the preoperative medication of choice in elderly and poor-risk cases. Also, children tolerate the drug very well (0.25-0.5 mg. per lb. of body weight). Occasionally, dryness of the mouth and blurring of vision occur and are the only known side effects. It easily replaces the barbiturates and also gives an analgesic effect.

Meperidine is a central analgesic but not much of a sedative; it is vagolytic (spasmolytic on smooth muscles), produces amnesia, does not markedly depress respiration, inhibits secretions, does not depress cough reflex, and has no serious side effects. Occasionally, it might cause nausea or dizziness, but with the use of chlorpromazine and promethazine, this rarely occurs.

Scopolamine and atropine inhibit structures which are postganglionic, or parasympathetic. By these drugs, the smooth muscles of the bronchi and bronchioles are relaxed. This increases airway and residual air and thus causes deep respiration. It also diminishes laryngospasm. Scopolamine stimulates respiration; atropine does so less well. Both drugs counteract morphine and barbiturate depression on the vital centers. Scopolamine is tranquilizing, causing some drowsiness; it is not hypnotic; it causes some euphoria, perhaps amnesia and fatigue (centrally depressant), and also nonanalgesic sedation. Therefore, if the patient experiences pain, this might cause excitement, delirium, or even convulsions (mainly in older patients), even with the combination of meperidine as an analgesic. Because of this, it is advisable to use atropine for older patients rather than scopolamine. Atropine stimulates the higher cerebral centers and the medulla, and it inhibits the salivaries and the glands of the respiratory tract and skin. Atropine may slow down the heart rate by central effect. It prevents a typical cardiac (vagus) arrest, or cardiac reflexes, which might occur from anesthetic inhalation, irritation, stimulation of the carotid sinus, etc. Atropine alone and in combination with papaverine are life saving for this kind of

accident, in that atropine removes the vagal influence on the heart. It also counteracts peripheral dilatation, and blood pressure drops, which is desirable with premedication of phenothiazines.

Our suggested premedication is 75 to 100 mg. chlorpromazine (the night prior to endoscopy), 25 to 50 mg. chlorpromazine, 25 to 50 mg. promethazine, 50 to 100 mg. meperidine, and 0.32 to 0.4 mg. scopolamine or atropine. These last four are given one hour prior to endoscopy, preferably by injection. If exact timing is possible, one-half of the dose of chlorpromazine and one-half of promethazine are injected 2 hours prior to endoscopy; the remainder of these two doses and meperidine, with scopolamine or atropine, are given on call to the operating room.

The patient's appearance after this premedication is as follows.

1. He is asleep and unconscious.
2. The skin is pale, but warm; lips and eyelids are of good color.
3. There is decreased but regular respiratory rhythm.
4. The pulse is strong, at a rate of about 90.
5. Blood pressure may be 10 to 30 mm. Hg below the patients' normal blood pressure.
6. The patient reacts to strong excitation and commands and then falls back to sleep.

The patient remains in this stage of hypometabolism for 6 to 10 hours, and, although observation is important, he should not be disturbed. No analeptics must be used if there is concern about the patient. Ephedrine and caffeine are the only drugs to be used. Any analeptics will increase the need of the body for oxygen, which is already in a low concentration at this stage of low metabolism and must not be lowered.

Topical anesthetics available at this time, are as follows:

1. Cocaine may be administered in a maximal dose of 1/10 of 1 gm. (e.g., 1 cc. of a 10% solution).
2. Tetracaine hydrochloride (Pontocaine) may be given in a maximal dose of 2.5 cc. of a 2% solution. Tetracaine hydrochloride is a longer-acting anesthetic, said to be more dangerous in causing toxic reactions than cocaine. Caution is to be used if the mucosa of the respiratory or digestive tract is traumatized in any place. This applies to allergic or hyperthyroid patients as well as patients with heart disease.
3. Lidocaine (Xylocaine) is said to be the least toxic, based on experiences during the last few years, and it also can be used on children. It is used in a 1% to 2% solution. But some patients, not allergic to procaine, are allergic to lidocaine.
4. Hexylcaine (Cyclaine) is used in a 5% solution, and is as safe as lidocaine.

In general, all topical anesthetics have to be used very cautiously, and it is most important to apply them in small amounts and low percentages over a period of time. Also, do not use the strongest concentration but, rather, dilute the recommended solutions to one-half or one-fourth strength. Isotonic saline is used for dilution. Special attention has to be paid to the sprays which are in use, since it is difficult to measure the amount of anesthetic applied. It has been stated that toxic reactions are rarely due to idiosyncrasy or allergy. Most toxic reactions are due to too high a blood level of the anesthetic. Therefore, slow application and low percentage are most important. From every anesthetic applied to the respiratory tract, a great deal goes down into the alveoli, and the absorption by the alveoli, as experiments by Steinhaus have shown, equals intravenous application. This gives us an idea of how dangerous it is to "soak" the patient with topical anesthesia. In the Philadelphia Endoscopic Clinics, these anesthetics are given in a mixed form. One might think this combination more dangerous in causing toxic reactions, but the amount of each anesthetic is small and does not easily permit severe toxic reactions, which are the ones which most concern us.

The following drugs are used in combination.

1. Cocaine 4% and 10%.
2. Tetracaine hydrochloride 1% and 2%.
3. Lidocaine 1% and 2%.

For esophagoscopy, they give 1 to 2 cc. 2% tetracaine hydrochloride spray.

For laryngoscopy, they give 1% to 2% tetracaine hydrochloride spray and 10% cocaine via laryngeal canulla.

For bronchoscopy, they give 1% tetracaine hydrochloride spray for the throat, 4% cocaine (1 cc. into the larynx), 2% lidocaine (8 cc. for the tracheobronchial tree, 2 cc. at the time).

For children from 10 years of age on, 2% lidocaine can be admistered to the larynx. For younger children, no laryngeal anesthesia is used but, through the laryngoscope, for bronchoscopy, lidocaine is applied into the trachea as follows: In children 2 to 6 years of age, 2 to 4 cc. 1% is given. Children 6 to 10 years of age receive 2 to 4 cc. 2%.

Toxic Reactions

Toxic reactions are rare, but one has to know about the symptoms and has to be prepared to counteract them immediately. The severest reaction possible is when, after a few drops of an anesthetic is applied, the patient dies suddenly. In the less severe reactions we have different stages. The symptoms can be separated into four stages, which are, (1) the patient is usually euphoric and talkative, (2) the patient becomes apprehensive and restless and may feel short of breath, (3) incoordination appears (twitching of hands) and the patient becomes less responsive, and (4) convulsions occur and respiration becomes irregular and finally ceases. Prompt recognition and action are of utmost importance.

Reactions are most liable to occur 10 to 20 minutes after the anesthetic has been applied, but they can also occur after the procedure and even outside the office, waiting room, or operating room. Therefore, it is wise to keep the patient under observation until it is safe to send him away. In more than 400 cases in which phenothiazines were used to premedicate the patient, no toxic reactions occurred when endoscopies or bronchograms were done with the mentioned topical anesthetics.

Treatment of Toxic Reactions

In any such accident, the most important thing is to establish a good airway and apply oxygen, if necessary and possible, via intubation and positive pressure respiration; then give barbiturates. Give 2 to 4 gr. of sodium phenobarbital, a 2.5% solution, subcutaneously if the toxic reaction is mild, intravenously if the reaction is strong. No analeptics are to be given, as mentioned before, because they increase the oxygen demand. A list of emergency drugs follows. These should be available in any ENT office, clinic, operating room, roentgen department; in fact, anywhere endoscopies or bronchograms are performed.

Emergency Drugs

1. Epinephrine chloride, 1 cc.=1 mg.; 30 cc. vial.
2. Epinephrine chloride, 1:1,000; 1 cc. ampule.
3. Atropine sulfate, 1 cc.=1/150 gr.; 20 cc. vial.
4. Diphenhydramine (Benadryl), 1 cc.=10 mg.; 10 cc. vial.
5. Caffeine sodium benzoate, 2 cc.=7½ gr. or 0.5 gm.; 2 cc. ampule.
6. Calcium chloride, 10 cc.=1 gm.; 10 cc. ampule.
7. Lanatoside C (Cedilanid), 2 cc.=0.4 mg.; 2 cc. ampule.
8. Hydrocortisone (Hydrocortone), 100 mg.=20 cc.; 20 cc. ampule (to be used only in 500 cc. isotonic saline or dextrose).
9. Ephedrine, 1 cc.=50 mg.; 1 cc. ampule.
10. Picrotoxin, 0.3% solution; 20 cc. vial.
11. Quinidine hydrochloride, 0.18 gm.=1.5 cc. ampule.
12. Phenobarbital sodium, 2 gr. per ampule; 1 ampule.
13. Strophanthin-G, USP 0.25 mg.=1 cc.; 2 cc. ampule.
14. Chlorpromazine, 25 mg.=1 cc.; 1 cc. ampule.
15. Thiopental sodium, 2.5 solution; 20 cc. syringe.

It is wise to have oxygen available within reach and also to have a syringe with sodium phenobarbital, which is drawn into the syringe, wrapped up sterilely in a drawer for immediate use.

Postendoscopic Orders

If topical anesthesia is used, the patient must have nothing by mouth for one to two hours or until the anesthetic wears off. This will preclude possible aspiration. Then he may return to preoperative routine, that means all medications, etc., which were given before. The same is true when general anesthesia is used, but here we must have restoration of all vital signs as well. With the kind of anesthesia described, or with thiopental, succinylcholine, and artificial respirator, the postoperative course has, in our experience, been uneventful. No complications occurred on more than 400 endoscopies. However, the patients must be recovered from their preoperative medications before resumption of their usual ones, except where otherwise indicated.

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Primary Repair of Defects Following the Surgical Removal of Tumors of the Face (Auricle)

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Introduction

The original films were in backlighted color transparencies. Only that portion of the exhibit relating to the auricle is herein displayed. The remainder * consists of the technique of repair after the removal of tumors of the lips and various areas of the face.

The cartilage of the auricle is an excellent barrier to the spread of cancer by the lymphatics and is seldom directly involved in early cases. The segment of auricle directly opposite an involved site can therefore often be considered as removed from it, not by the distance through and through the auricle, but by the linear distance from the site of the lesion to the edge of the ear and then around the opposite side to a point opposite.

In deciding upon the type of surgery for the cure of cancer of the auricle and its primary repair, the surgical concept adopted is therefore that of the structure of the external ear being a single flat surface with the internal and external aspects separated from each other and laid out to form the adjoining halves of a flattened structure. This makes it possible to safely salvage large segments of the auricle which are used for reconstruction of the organ. There is probably no structure in the body more difficult to reconstruct (or one in which the repair is less satisfactory) than the auricle, particularly from the standpoint of cosmetic values. The concept above advanced and herein illustrated provides additional opportunities for satisfactory repair without appreciably increasing the likelihood of recurrence.

The cartilage over the excised area should, however, always be included with the specimen and removed, since the perichondrium of the involved surface cannot, with safety, be separated from it.

Three distinct types of lesions are presented. These are of the margin involving the helix, those of the anterior surface, and those of the posterior surface.

The first case demonstrates involvement near the margin. Through and through excision of a segment of the auricle is therefore required, and neither skin surface can be preserved. Primary reconstruction is accomplished by planned incisions and the use of residual remnants. In this instance the antihelix is used to replace the excised portion of the helix.

The second case represents resection of carcinoma of the posterior surface with surgical preservation of the external surface of the skin. Repair is accomplished without the use of cartilaginous support except for a narrow rim which had been retained about the margin. The normal convolutions of

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the auricle are preserved by proper pressure-packing during healing. Evidently fibrous tissue forms in place of the cartilage and satisfactorily preserves the external contour.

The third case represents involvement of a portion of the external surface which has been excised together with underlying cartilage. The posterior skin surface is preserved and used to line a large, full-thickness, pedicle flap taken from the scalp behind the ear. This is swung forward under the retained helix to replace the excised area and detached a few weeks later when an independent blood supply has been established.

The fourth case of auricular repair is of a small lesion in the concha. This was removed by through and through excision and repaired by the use of a small sliding flap taken from the area of the mastoid.

As an alternative to the above, it is to be noted that excellent repair of small lesions can often be accomplished by through-and-through excision and the use of full-thickness free grafts taken from behind the ear.

CASE I

Fig. 1.—Lesion involving extensive area of external surface of auricle.

Fig. 2.—Outline of area of through-and-through excision sparing segment of antihelix.

Fig. 3.—Involved segment partially excised.

Fig. 4.—Excision completed sparing upper and lower fragments of helix and medial portion of the antihelix.

Fig. 5.—Antihelix being separated from bed for repositioning.

Fig. 6.—Upper and lower segments of helix sutured to antihelix.

Fig. 7.—Left: Postoperative results after two weeks. Right: Postoperative results after six months.

CASE II

Fig. 1.—Ear folded forward demonstrating large carcinoma of internal surface.

Fig. 2.—Area of excision outlined.

Fig. 3.—Excision carried through skin and cartilage.

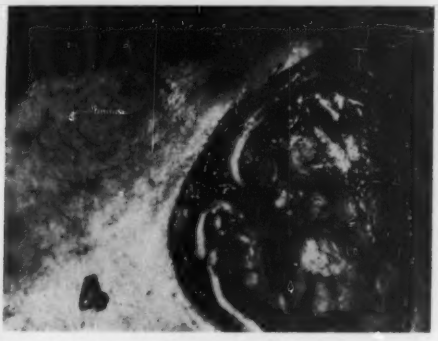

Fig. 4.—Specimen removed. Posterior aspect of skin of external surface presenting in the depth of the wound.

Fig. 5.—Pocket created posteriorly to provide postauricular sulcus.

Fig. 6.—Auricle resutured in situ.

Fig. 7.—Postoperative cosmetic result after four months.

Fig. 8.—Excised specimen including skin, perichondrim, and underlying cartilage.

CASE III

Fig. 1.—Carcinoma of external surface of auricle.

Fig. 2.—Lesion widely excised including underlying cartilage.

Fig. 3.—External aspect of skin of internal surface preserved and presenting.

Fig. 4.—Retained skin of posterior surface severed at helix to provide lining for pedicle flap.

Fig. 5.—Pedicle flap outlined on scalp.

Fig. 6.—Pedicle flap freed.

Fig. 7.—Apex of pedicle flap swung into position overlying raw surface of skin of posterior aspect of the auricle. Traction sutures in latter to insure proper positioning.

Fig. 8.—Apex of flap sutured to anterior margin of primary incision.

Fig. 9.—Donor site approximated after extensive undermining.

Fig. 10.—Completed first stage. Flap in situ. Severed margin of helix sutured to create tube.

Fig. 11.—Two weeks postoperative, external view.

Fig. 12.—One month postoperative. Internal aspect demonstrating neck of pedicle flap.

Fig. 13.—Posterior limit of flap delineated.

Fig. 14.—Freed superior segment of flap sutured to helix.

Fig. 15.—Immediately prior to final stage.

Fig. 16.—Marking posterior limit of flap at point of severance.

Fig. 17.—Residual of flap brought forward into position for suturing.

Fig. 18.—Posterior view. Flap freed *in toto*.

Fig. 19.—Cosmetic result, external surface, after four months.

Fig. 20.—Cosmetic result, internal surface, after four months.

CASE IV

Fig. 1.—Relatively small lesion involving external surface of antihelix.

Fig. 2.—Through-and-through excision of involved area.

Fig. 3.—Sliding flap created from scalp posterior to auricle and widely undermined.

Fig. 4.—Flap drawn forward to position for suturing.

Fig. 5.—Anterior limit of flap sutured to anterior limit of excision. Area of helix sutured to close skin edge.

Fig. 6.—Postoperative result after six weeks. Primary stage healed.

Fig. 7.—Posterior limit of flap severed and attached to posterior surface of excised area after denuding the latter.

Fig. 8.—Posterior view after completion of second stage.

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Audiology Section

JOSEPH SATALOFF, ASSOCIATE EDITOR

Hearing Problems in Athetoid Cerebral Palsy

Preliminary Report of Case Findings

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Workers in the field of speech and hearing therapy, particularly those concerned with the rehabilitation problems of the cerebral palsied, have often been confronted in their perusal of the literature by the term "athetoid deaf." Various attempts have been made to investigate the hearing impairment which appears to be associated with athetosis. As a result of clinical observations of both the test situations and the audiometric findings on a group of subjects with cerebral palsy for whom the primary diagnosis was athetosis, the authors felt a need for more extensive investigation into the nature of this hearing loss.

This is a preliminary report and concerns itself primarily with two aspects of the investigation. The authors were interested in determining (1) whether there is a true loss of hearing sensitivity in "athetoid deafness" and (2) whether there is an audiometric configuration characteristic of the "athetoid deaf."

A number of writers have described the type of deafness found in athetoid cerebral palsied patients. In 1941, Phelps [1] reported that hearing defects in cerebral palsied patients are common, especially in those with athetosis. He found this loss affected primarily the high frequencies. Goodhill [2] reports a similar occurrence of deafness in the athetoid subgroup. Of a group of forty-one studied, thirteen cerebral palsied children with athetosis were found to have significant hearing impairments. Cavanaugh [3] found 6 cases of unsuspected deafness in a group of 124 babies with a history of Rh incompatibility. More recently, Rutherford [4] reported an inconstant loss of hearing in cerebral palsied children, particularly those with athetosis. She attributed the failure to hear consistently, not to pathology of the ear, but to a lesion in the central nervous system. Fisch [5] reported a survey of deafness conducted in three different types of schools for cerebral palsied children. Eighty-nine children were tested, and 20% showed a hearing loss which Fisch claimed could cause considerable handicap. Markwitz [6] also noted the occurrence of perceptive losses of hearing in cerebral palsied cases and reproduced a typical audiogram found in these patients which is of the same bilateral, high frequency type reported by the other workers in the field.

The pure-tone audiometric findings are presented for 18 cerebral palsied subjects on whom a diagnosis of athetosis was made by the examining neurologist. These subjects represent a selected group of patients: The basis of selection was a suspected loss of hearing. Each audiogram represents the cumulative result of several test sessions with each subject.

The test situations varied slightly from subject to subject but included, in the cases

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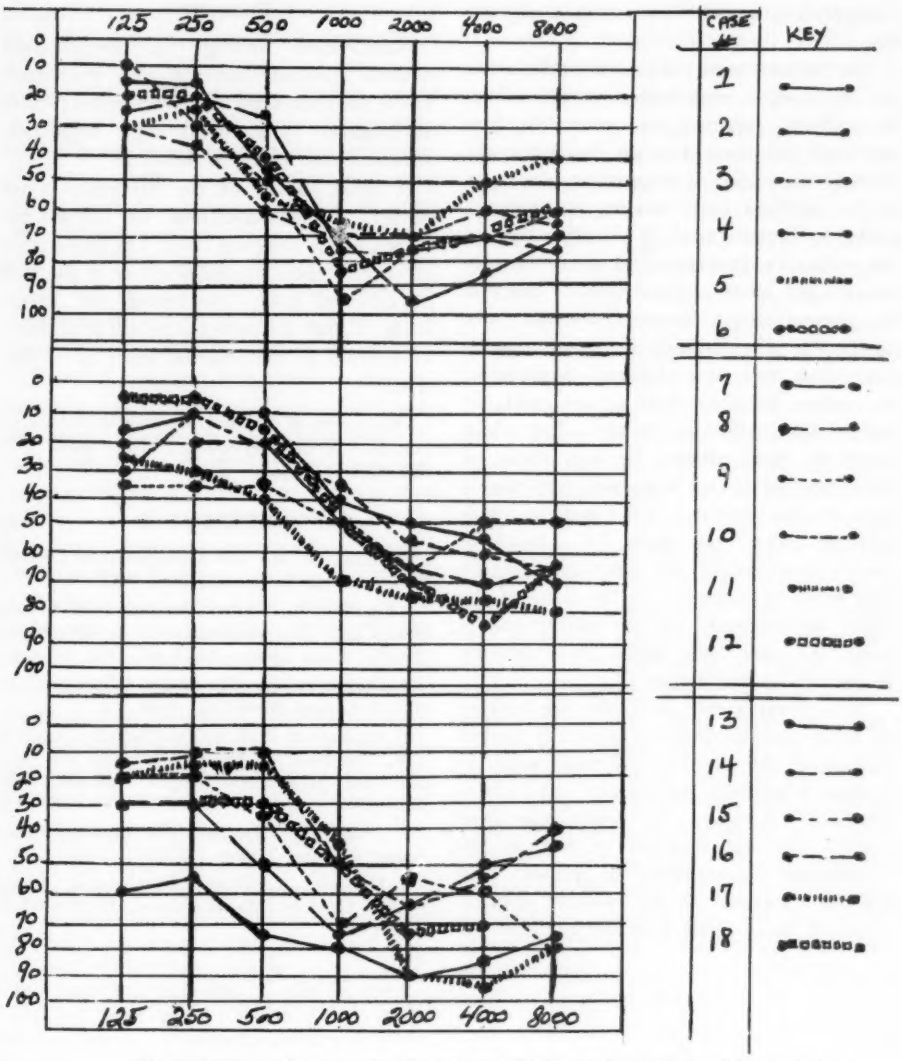
of the children examined, an initial presentation of various sound stimuli (music, speech, noise, etc.) in a sound field *and* through earphones for conditioning purposes; then threshold readings were obtained for 125, 250, 500, 1,000, 2,000, 4,000, and 8,000 cps. For the adolescents and adults examined, the testing procedure followed standard audiometric techniques except where it was necessary to modify the response pattern in accordance with the motor disability involved. The age range for the subjects examined was 9 to 37, with a mean age of 18.66. All testing was performed in sound-treated rooms (where quiet conditions prevailed) with use of standard pure-tone audiometers.

The air-conduction audiograms for the left ears of the 18 subjects tested are shown in the Figure.



Air conduction audiograms for the left ear of 18 athetoid cerebral palsied patients.

The type of loss which was found in the athetoid cerebral palsied population tested was a bilateral, high frequency, symmetrical, sensorineural hearing loss.

This study indicates that (1) this hearing loss represents an actual reduction in hearing sensitivity as determined by the excellent inter and intra test-retest consistency, and that (2) there is sufficient similarity of audiograms from subject to subject to raise the possibility of a characteristic configuration within this selective population.

The authors were surprised to find that the audiometric examination performed on the subjects reported was often the first test that had been done to determine the hearing sensitivity of the patient. In many of the cerebral palsy centers in existence today, a "hearing test" is a routine part of the evaluation procedure. Most of the adolescent and adult cerebral palsied cases in the present group, however, did not have the benefit of a complete diagnostic evaluation when they were children. Because of the nature of their hearing loss and the compensatory skills in speech reading which many of these patients develop, many of these hearing losses were not suspected—even by the parents. Since patients with cerebral palsy may often be delayed in speech development and since their speech may often be defective on the basis of the motor involvement, we can readily understand the ease with which these hearing losses can be overlooked.

Clinical experience in testing the hearing of these patients shows a generally abrupt arousal of the auditory threshold with responses frequently characteristic of recruiting ears. In view of the recent intensified clinical and experimental interest in the recruitment phenomenon, the authors have become interested in the possible implications of these clinical findings. There is indication here for more intensive testing in this area.

There appears, further, to be a striking visual similarity between the audiograms of the athetoid cerebral palsied children reported in this study and those of patients with advanced acoustic trauma. Here again the authors are concerned with the necessity to investigate further this area of similarity.

Summary

Audiometric findings on 18 athetoid cerebral palsied patients are presented. These subjects show a characteristic picture of bilateral, symmetrical, high frequency, sensorineural losses of hearing.

A brief survey of the literature is included. Recommendations for future research in the area are cited. The importance of an awareness among workers in the field of cerebral palsy concerning the occurrence of high frequency sensorineural losses of hearing in the athetoid cases is emphasized.

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Clinical Applications of the Temporary Threshold Shift

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Although the inherent characteristics of poststimulatory auditory fatigue have been studied for some time, it has not been until the last decade that interest has been shown in a relatively new method of measuring auditory threshold changes due to sound stimuli. A number of specific clinical techniques have been reported for discerning temporary shifts in threshold that occur during periods of sustained-tone stimulation. The results of studies carried out with two of these techniques have led to a number of interesting practical speculations that have been applied to the clinical evaluation of abnormal hearing.

Dix, Hallpike, and Hood [1-5] have stressed two major factors which discriminate poststimulatory fatigue from abnormal loudness level losses that occur during periods of tone stimulation. The first of these is that the amount of fatigue following a tone stimulus is dependent on the physical magnitude of the stimulus. However, changes in loudness level that occur during sound stimulation by intermittently balancing the loudness of a control tone in one ear with the stimulus tone in the other seem to be independent of intensity. The second factor emphasized is that if the intensity of a fatiguing stimulus is steadily raised from threshold to a level at which it is no longer audible, is then interrupted, and is then reapplied immediately, almost complete sensitivity restoration occurs for that tone. The effects of poststimulatory fatigue are more persistent, however, and recovery is much slower.

The above three authors termed the presence of a temporary threshold shift (TTS) that occurs during sustained-tone stimulation as evidence of "per-stimulatory adaptation." They compared the phenomenon directly to the adaptation state in the single sensory receptor, described by Mathews [6] as a high-frequency discharge, or "on-effect," occurring approximately 0.2 second after the onset of the stimulus, followed by a slow decline in response (adaptation), and a short rest period. The onset of another stimulus gives the same on-effect, but a more accelerated adaptive response, depending on the length of the rest period.

Having placed the anatomical locus of auditory adaptation in the cochlear end-organ, Dix, Hallpike, and Hood proposed that *abnormal* adaptation, or "pathological relapse" (a TTS measured during tone stimulation, but occurring to a greater degree than normal), is as much a manifestation of an abnormal physiological state of the organ of Corti as is the presence of loudness recruitment. The natural consequence of this reasoning was an attempt to develop a clinical means of detecting and measuring the amount of per-stimulatory adaptation in abnormal ears for the purpose of providing an audiometric technique that could be applied to the differential diagnosis of cochlear involvement.

In 1955, Hood [3] reiterated the fact that adaptation is independent of the intensity

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of the stimulus and emphasized that it may occur at threshold levels. As an example, it would be assumed that a normal hearing subject, or one with a conductive type hearing loss, would detect a sustained tone at a level 5 db. above threshold for an indefinite period. However, in those ears with losses due to impairment of cochlear function, tonal sensation would disappear completely after a few seconds of sustained stimulation and the sensation level of the stimulus would have to be raised 20 or 30 db. before a continuous response could be obtained. Such a measure, as described by Hood, could be carried out quite simply with a pure-tone audiometer.

Carhart [7] described such a technique in 1957 and called it the "Threshold Tone Decay Test." It consists of presenting a sustained tone from a pure-tone clinical audiometer at the subject's threshold level for a period of at least one minute. If the tone is perceived at this level, or a maximum of 5 db. above original threshold, for the entire period, no abnormal adaptation is judged to be present. The latter result is expected in normal ears and in those with a pure conductive type loss. If, however, the signal fades into inaudibility before the one-minute period of stimulation is completed, the tone is immediately increased 5 db. and a new one-minute stimulus period is initiated. This procedure is continued until an intensity is reached at which the tone is heard without interruption for a full minute. The presence of a continually higher threshold shift was originally presumed to be evidence of abnormal adaptation and, in conformance with the reasoning of Dix, Hallpike, and Hood, pathognomonic of a cochlear lesion.

In discussing certain clinical results obtained in six abnormal ears, however, Carhart cautioned that due to the inconsistent nature of his findings, one cannot conclude that the test is solely indicative of cochlear involvement when abnormal threshold shifts are detected. This conclusion was somewhat amplified and supported by the clinical findings of Thompson and Hoel.[8] They found certain degrees of abnormal TTS in 10 of 15 ears with cochlear pathology due to Ménière's disease or toxic labyrinthitis. However, they reported that a much severer and more bizarre pattern of threshold shift was present in three of a group of seven patients with *retrocochlear* lesions than in those with cochlear involvement.

On the basis of the above clinical results, there seems to be support for the observation that the "tone-decay" test does not singularly distinguish cochlear lesions, even though the inherent premise of the test is based upon the discrimination of per-stimulatory auditory adaptation. Nevertheless, the detection of distinctly abnormal TTS patterns with this test in retrocochlear lesions is worthy of further investigation.

Since 1952, a number of studies have been made on abnormal ears employing the technique of recording threshold levels at single frequencies with the use of an automatic audiometer. In certain types of hearing losses, interesting patterns of threshold shifts appear over relatively short periods of time, usually no longer than three minutes. In normal ears, one would expect no more than a 5 db. variation from the original threshold level obtained.

Lierle, Reger, and Kos [9-12] have demonstrated quite consistently that when applying this technique over a maximum time of three minutes very few shifts in threshold are found in ears with cochlear lesions demonstrating loudness recruitment. However, various degrees of significantly marked threshold adaptation have been consistently observed in patients with losses due to retrocochlear lesions, such as acoustic neuroma and eighth-nerve atrophy. Palva [13] reported no significant TTS using this method in four cases showing positive recruitment.

Jerger, Carhart, and Lassman [14] recently confirmed the findings of Lierle, Reger, and Kos by presenting very bizarre patterns of TTS during automatic recordings of

threshold in two cases of acoustic neurinoma. They concluded that threshold tracings obtained by them in cochlear lesions are such that they fail to support the contentions of Dix and Hood with regard to the locus of the lesion in cases of abnormal adaptation.

It is interesting to note in this connection that Dix and Hood[1] briefly mentioned similar tests that they performed on two cases with Ménière's disease and on an undisclosed number of subjects with eighth-nerve lesions. They found abnormal shifts in threshold (a maximum of 15 db. in the cochlear losses) in both pathological entities and felt that abnormal adaptation does not always occur in recruiting ears. They therefore concluded that the test cannot be used as a measure of recruitment.

In summary, it would seem that the fundamental conflicts observed in the clinical data obtained with the two techniques described above must be justified if we are to conclude that tests of per-stimulatory adaptation have diagnostic value in a clinical context. On the one hand, we have statements made to the effect that the presence of abnormal adaptation, which can be measured as a temporary shift in threshold occurring during tone stimulation, is indicative of a cochlear lesion, although it is not necessarily present in all cases demonstrating loudness recruitment. Yet a study of the clinical results obtained in two techniques which purport to measure this phenomenon show definite inconsistencies, with various degrees of TTS demonstrated in both cochlear and retrocochlear pathology.

It is the purpose of this study to attempt to gain further insight into the discrepancies just mentioned by studying clinical data obtained with both clinical techniques on the same ears of normal subjects and patients with various types of hearing losses.

Procedure and Results

Normal Ears.—In order to confirm the basic normal patterns expected in the two procedures investigated and to compare the two tests under normal conditions, the Threshold Tone Decay Test (hereafter referred to as Test A) was administered to one normal ear of each of 20 subjects at 250, 500, 1,000, 2,000, and 4,000 cps. The only procedural variation from that of Carhart[7] was that the first tone presentation for each frequency was presented at a sensation level of 5 db. rather than at threshold.

Each subject was then instructed identically in the task of bracketing the tone presentations at threshold on a Reger version of an automatic audiometer[15] (Test B). Each two-minute frequency presentation was begun at a subliminal level at a constant attenuator speed of 2.5 db. per second, and recordings were made by means of an electrically heated stylus on heat-sensitive paper.

None of the 20 subjects exhibited a TTS with Test A greater than 5 db. at all frequencies but 4,000 cps. For the latter tone, three subjects showed a maximum shift in threshold of 10 db., and in one subject there was a shift of 20 db.

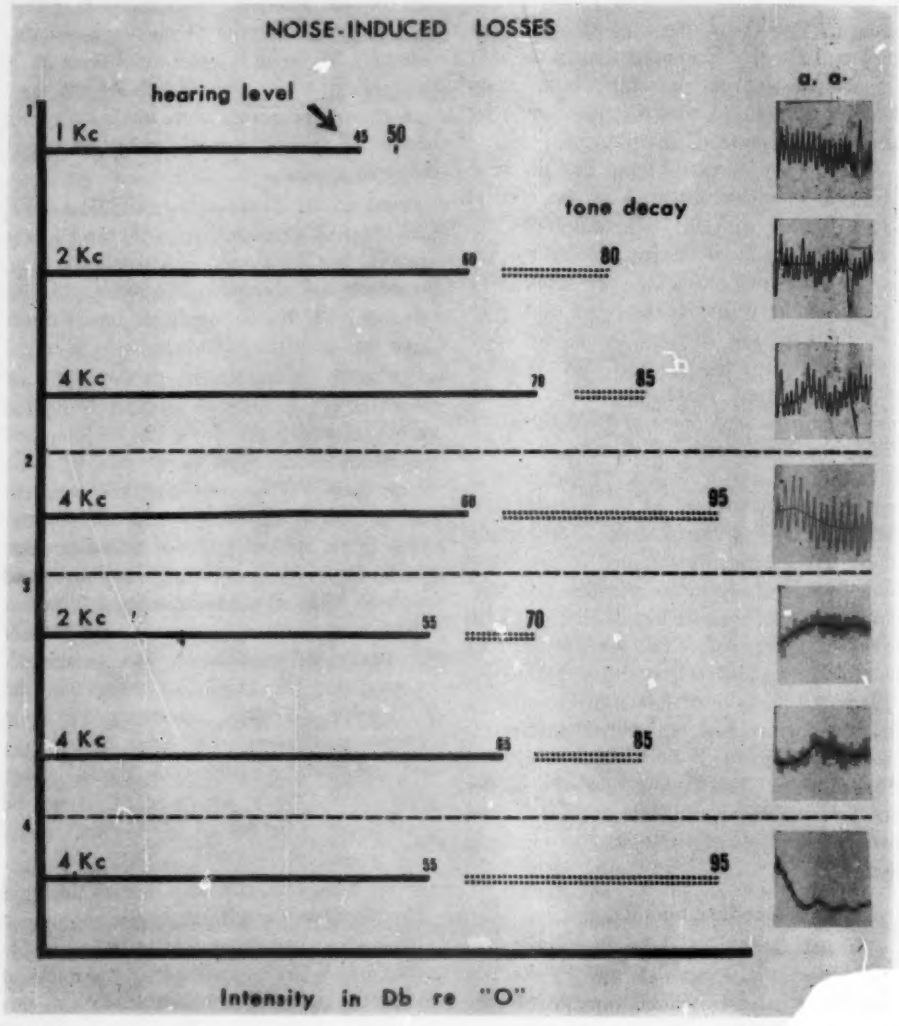
Although the midpoints of the width of the threshold excursions in Test B dipped an average of 5 db. from the midpoint of the width of the first excursions in some cases, there was no consistent and progressive lowering of threshold in the normal ears. Some subjects showed transient temporary shifts close to 20 db., but threshold in these cases characteristically followed a direction towards the original level before the period of stimulation was completed. In assessing the results of measuring the TTS using automatic audiometry, the basic criteria was, then, that only progressive and consistent elevations of threshold beyond 5 db., with no recovery, could be considered to be out of the normal range.

Abnormal Ears.—The criteria for selection of abnormal ears were somewhat rigid in order to insure adequately the acceptance of cases in which there was little reasonable doubt of the otological and/or neurological diagnosis. One ear of each of 13 subjects

was fully tested. Three of these were cases of pure conductive type losses due to chronic otitis media in one and clinical otosclerosis in the remaining two. The latter diagnosis was confirmed during stapes-mobilization surgery. The results of the two tests were comparable to those in the normal group, meeting the criteria of normalcy previously established. There was no TTS greater than 5 db. on either test.

Seven patients with perceptive losses and evidence of cochlear involvement as determined otologically and audiometrically were tested. Of these, four cases gave a typical

Fig. 1.—Pure-tone thresholds and results obtained at the abnormal frequencies in Cases 1 to 4. All intensity levels are in decibels *re* audiometric zero. The degree of TTS (or "tone decay"), as measured with Test A, is detailed immediately after the hearing level and indicates the level at which the subject heard the test tone for one full minute. Results obtained with Test B (automatic audiometry) are arranged at the extreme right of the figure. A solid line is drawn through the approximate midpoints of the excursions to indicate threshold changes over the two-minute recording time.



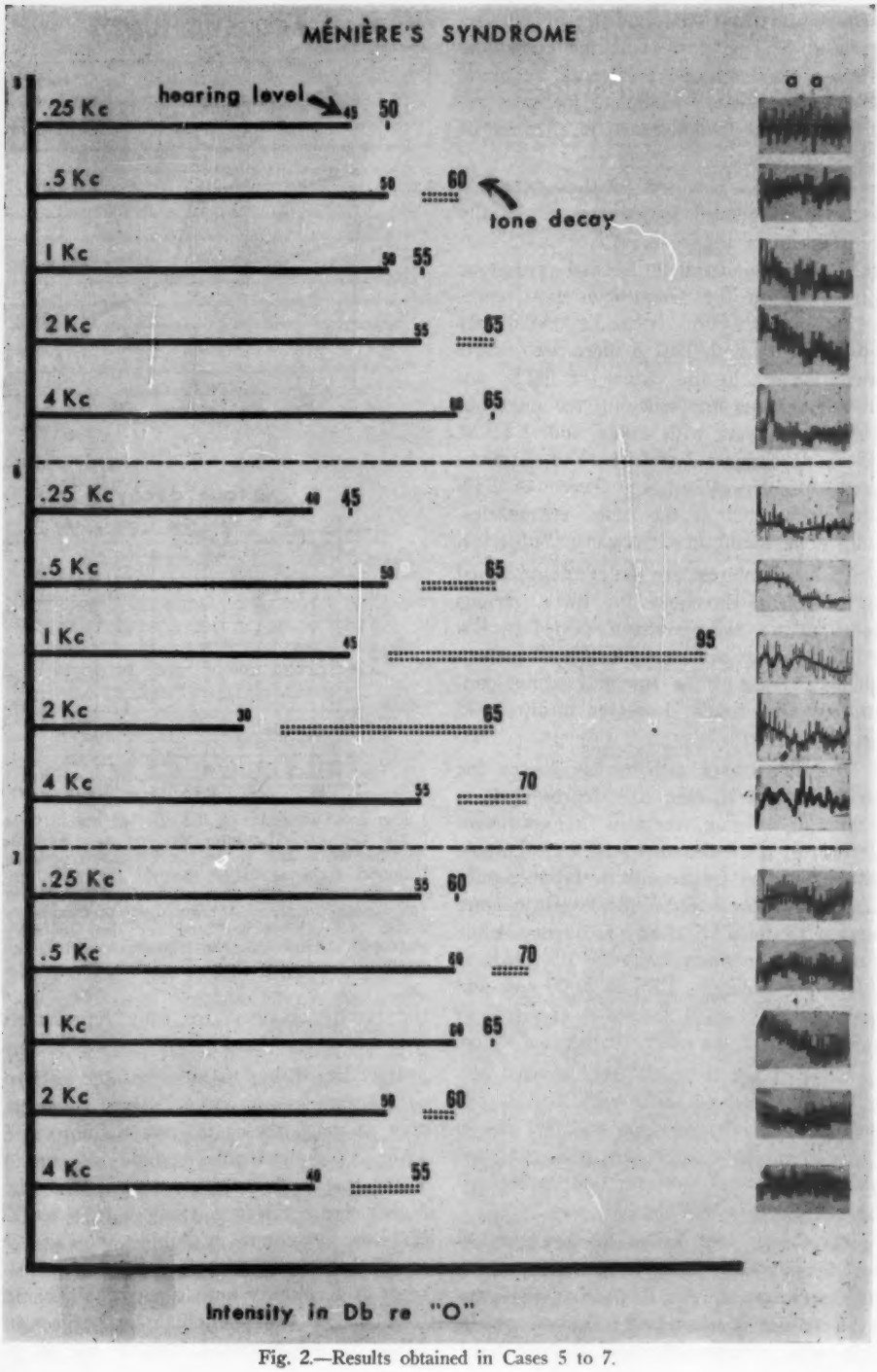


Fig. 2.—Results obtained in Cases 5 to 7.

history and functional evidence of a noise-induced hearing loss, and the remaining three were diagnosed as due to unilateral Ménière's disease. Complete loudness recruitment was demonstrated in all three of the latter cases.

The results obtained in those subjects with noise-induced losses are graphically reproduced in Figure 1. All of these four subjects demonstrated normal pure-tone thresholds at the frequencies not represented in this figure. It can be immediately observed that with Test A there is a definite inconsistency in the extent of TTS, not only from one frequency to the next but between subjects, with a maximum TTS of 35 db. in Subject 2 and of 40 db. in Subject 4. Considerably lower degrees of TTS are represented at the other frequencies, with none found at 1,000 cps in Subject 1.

Of equal interest are the results obtained in recording threshold for these various tones over a two-minute period (Test B). Although there are small degrees of pattern changes, none of the tracings exhibit continuous and steady decreases in threshold sensitivity.

The three cases with hearing losses due to Ménière's disease are represented in Figure 2. Again, there is no consistent pattern of TTS demonstrated with Test A, either between frequencies or between subjects. Subjects 5 and 7 displayed no more than a 15 db. TTS at any frequency, while Subject 6 demonstrated a 50 db. shift at 1,000 cps, a 35 db. TTS at 2,000 cps, and comparatively small threshold changes, or none at all, at the other frequencies tested.

None of the three subjects showed any abnormal threshold shifts with Test B, except for a moderate slope at 2,000 cps in Subject 5. This latter shift was not considered abnormal, however, within the criteria previously established.

Three cases with losses due to retrocochlear lesions were tested. All three patients had a unilateral cerebellopontine angle tumor confirmed at surgery. Because of the interesting patterns observed in these cases,

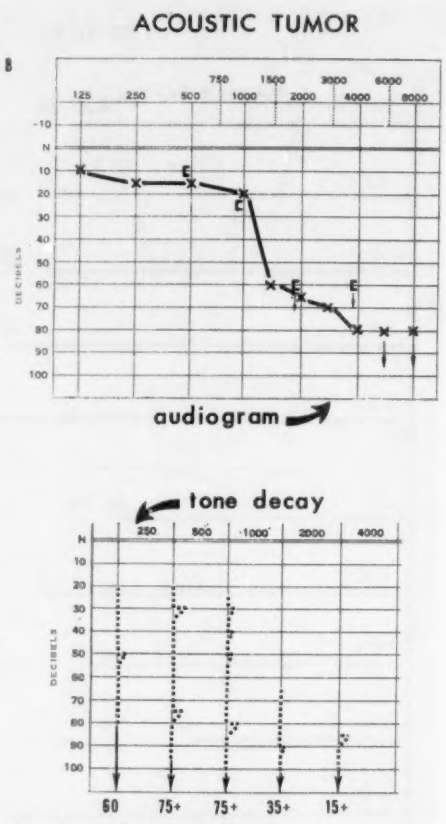


Fig. 3.—Audiogram of the affected ear in Case 8 and the detailed results obtained with Test A. The horizontal axis in the lower figure represents temporal divisions of 60 seconds for each frequency tested. Thus, if a tone were heard for a full minute, the dotted line would extend completely across the column indicated for the frequency employed. In this case, no tone was heard at any intensity for longer than 15 seconds.

the results obtained are fully represented in Figures 3, 4, and 5.

It is interesting to note that the pattern of the audiometric curve differed considerably among these patients. Subject 8 (Fig. 3) showed only a slight loss up to 1,000 cps, with an abrupt drop for the higher frequencies; a fairly flat 55 to 60 db. loss was found in Subject 9 (Fig. 4) up to 1,000 cps, with a gradual improvement in sensitivity until a normal threshold level at 8,000 cps was obtained; Subject 10 (Fig. 5) demonstrated a fairly flat 40 to

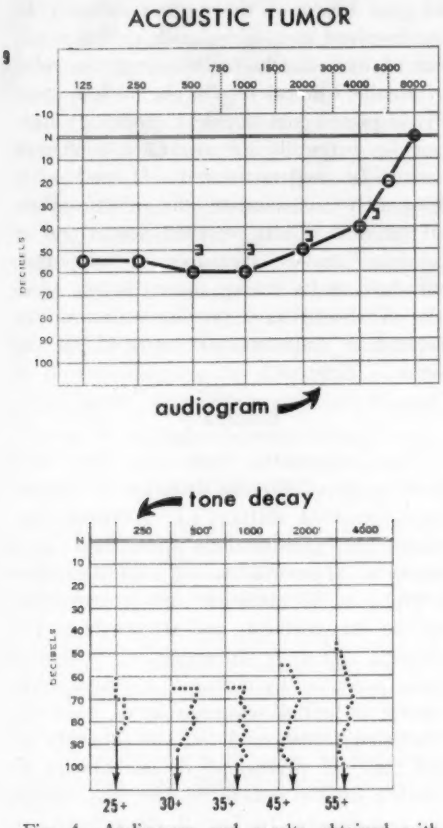


Fig. 4.—Audiogram and results obtained with Test A in Case 9.

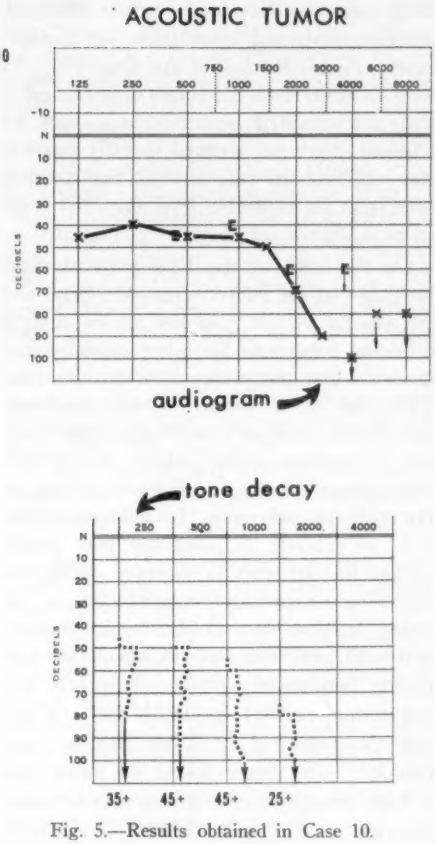


Fig. 5.—Results obtained in Case 10.

45 db. loss up to 1,000 cps with a gradual loss in sensitivity for higher frequencies, reaching a maximum at 4,000 cps and above. However, even though threshold sensitivity was variable, all of these subjects presented extremely bizarre patterns of TTS with Test A at all frequencies tested. There was no relationship to the tones presented at the maximum limits of the audiometer for longer than 30 seconds.

The results obtained by threshold recordings with Test B were also significant. The TTS was so extensive in Subjects 9 and 10 that they were unable to establish threshold at the limits of the audiometer (95 db. *re* normal audiometric zero). Subject 8, however, momentarily established threshold at 1,000 cps for 20 seconds but then rapidly adapted to a complete loss in sensitivity at the intensity limits of the audiometer.

Comment

From the practical standpoint, it would seem that either of the two techniques employed in this study can be applied to the task of detecting the presence of rapid sensitivity shifts to initially weak tones (with respect to threshold). It should be emphasized that the ear is really not subjected to a tone at a steady threshold intensity with time in Test B (automatic audiometry) but rather to a stimulus that is varied over a 10 to 15 db. range, or higher, according to the subject's reaction time and preestablished criteria. Clinically, however, one finds that there is very little

difference in the final result obtained, whether sustained attenuation or continuously variable intensities are employed. As long as continuous stimulation is presented and the activated neurones in a state of adaptation are not allowed to fully recover, the fact that the intensity of the stimulus tone is at an inaudible level does not seem to be a significant factor.

On the basis of the TTS patterns demonstrated in the subjects reported here, and the similar results obtained under slightly different conditions by other investigators, it seems that the presence of an abnormal TTS during a period of sustained-tone stimulation must rely more upon the integrity of elements of the auditory nerve itself rather than on the physiological status of the cochlear end-organ. In this connection, it is of interest to point out that almost no loss in sensitivity is observed during the recording of cochlear microphonics at the round window of animals during stimulation with pure tones up to intensities producing permanent damage. This fact was emphasized in 1951, by de Mare,[16] and was recently confirmed by Rahm, Strother, and Gulick.[17] The latter found no more than a 4 db. change in response in cats at sound pressure levels up to 68 db. (*re* 0.0002 microbar) over periods of up to 80 hours. If auditory adaptation were a characteristic property of cochlear physiology, one would expect to see evidence of this phenomenon in such studies.

It is not unwarranted to assume that the presence of partial tone decay of an inconsistent nature in ears with cochlear lesions may actually be due to a subclinical loss in the integrity of certain elements of the auditory nerve. One must always be aware of the fact that the presence of complete loudness recruitment is significantly related to cochlear dysfunction but does not preclude the possibility of retrocochlear involvement. The only real answer to this particular aspect of the problem must come from a comparison of the functional results of per-stimulatory fatigue tests and a histological study of the morbid anatomy of the involved ear. Since such evidence will not be immediately forthcoming, the value of further clinical results obtained in cases of suspected retrocochlear pathology that can be surgically or medically confirmed cannot be underestimated. If such data adequately substantiate the presumptions and clinical results reported herein and in previous studies, measures of temporary threshold shifts during sustained-tone stimulation should have positive value in the functional diagnosis of retrocochlear lesions.

Summary

Two audiometric techniques that have been proposed for the detection of temporary threshold shifts (TTS) during sustained-tone presentations were used in a group of 20 normal-hearing subjects and in a group of 13 abnormal ears representing middle ear, cochlear, and retrocochlear pathology. Test A consisted of sustained tones presented by means of a clinical audiometer at initial sensation levels of 5 db. Variations were made in the intensity of the tone, if necessary, in an attempt to reach a level at which the tone was audible for one minute. In Test B, the subject was asked to maintain threshold for a particular frequency over a two-minute period on an automatic audiometer.

The clinical data led to the following results:

1. In any ear, whether normal or abnormal, a TTS greater than 5 db. with use of either test is not characteristically found if the perceptive hearing mechanism is intact.

2. In some cases, but not all, of perceptive losses with evidence of cochlear involvement, a TTS may be present to a limited extent at certain frequencies with Test A. When a TTS is demonstrated with Test A in these subjects, it is almost always localized to higher, rather than to lower, frequencies. A TTS to any significant extent is not characteristic in these cases when Test B is used.

3. In three surgically confirmed cases of perceptive losses due to localized involvement of the auditory nerve (cerebellopontine angle tumors), extreme temporary shifts in threshold at all frequencies tested were highly characteristic in both tests.

It is concluded that the presence of abnormal auditory adaptation, as delineated by the two techniques used in this study, seems to be indicative of poor functional integrity of retrocochlear aspects of the auditory nervous system rather than to abnormal cochlear function. The application of these findings to the differential diagnosis of eighth nerve affections is emphasized.

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Case Reports

The Management of Intubation Granuloma

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If a patient calls on the laryngologist with complaints of a change in voice or speech, distinct hoarseness, difficulties in breathing, or even dyspnea and if laryngoscopy reveals a growth at the site of the vocal cord(s), the laryngologist will associate his findings with a host of possible conditions, such as polyps, fibroma, papilloma, neurofibroma, nodules, adenoma, lymphogranuloma, squamous-cell hyperplasia, and hyperkeratoma. Further, he will not be able to dismiss the possibility of some malignant growth, tuberculosis, etc. Among all those possibilities, the plain benign polyp will predominate in frequency. If this is the case, the etiology will usually remain obscure or doubtful, except for a more or less probable surmise that there has been abuse of voice or speech, professional or otherwise. The suggested management will be physical rest and silence, and sometimes removal of the growth for therapeutic and/or diagnostic purposes.

With the inception of intratracheal intubation for general anesthesia, however, a new clinical entity with a well-established traumatic origin made its clinical appearance. It has been named "granulomatous polyp of the vocal cords."

The intratracheal intubation is an ingenious and daring device and marks a step of doubtless progress on the way to a smooth and safe course of anesthesia. On the other hand, it is, in some circumstances, not wholly safe and the patient is sometimes liable, as can be seen from published reports,[6] to unpleasant complications of which the said granulomatous polyp is only one of the more innocent. It seems, therefore, worth while checking if and by what means those dangers and complications, including this polyp, can possibly be reduced or avoided. This is, if only in a limited degree, the objective of this paper.

According to Myerson,[7] the granulomatous polyp of the larynx is "an inflammatory tumor caused by trauma during intratracheal intubation for general anesthesia." In a later paper,[8] he observes that direct laryngoscopy, as performed for diagnostic or therapeutic ends, was seen to be followed by the development of that kind of polyp.

It is my observation, and no doubt an observation of other authors as well, that the growths in question, being at the beginning usually sessile and placed on a broad basis, more often do not develop into the shape of a pedunculated polyp. It is for this reason that Epstein and Winston, cited by Salinger,[9] rightly call them "granulomas" and not polyps. Taking all this into account, I would suggest that these growths be called postendoscopic granulomas or, in short, "endogranulomas."

The first case of intubation granuloma has, to my knowledge, been reported by Clausen,[1] in 1932. Since then such cases have become universally well known and have been described in fairly great numbers. I feel justified, however, in reporting my cases, because my observations as to location, prognosis, and, particularly, the management of them might prove useful to the reader.

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From the Chest Hospital in Ber-Yakow of Malben-J.D.C. Services in Israel. The American Joint Distribution Committee receives its funds in the United States from the United Jewish Appeal.

My observations have been collected at the 520-bed Chest Hospital of Malben, in Ber-Yakow, Israel, where I am an ear, nose, and throat specialist. I have observed 14 cases, 6 of which have been eliminated from this analysis because of insufficient histories or follow-ups. Here are the abridged histories of the remaining eight cases.

Report of Cases

CASE 1.—A 23-year-old woman. Bronchoscopy and mirror laryngoscopy showed no pathological findings in December, 1953. Tracheal intubation of three hours' duration, Feb. 1, 1954; mirror laryngoscopy, April 8, 1954; granuloma laryngis of the right vocal cord about 3 mm. in diameter with granuloma laryngis of the right vocal cord about 3 mm. in diameter with typical localization, slight hoarseness. No treatment except silence recommended. Mirror laryngoscopy on April 29, 1954; granuloma laryngis bigger in diameter. No special treatment. Last routine mirror laryngoscopy on Dec. 1, 1954; granuloma laryngis had disappeared; no pathological findings; voice normal. According to anamnesis taken from patient it seems probable that some time ago she had one day, spontaneously, coughed out the growth.

CASE 2.—A 27-year-old woman. On admission to this hospital, patient gave a history of thoracotomy for TB of the lungs which was performed (abroad) in general anesthesia one year earlier; tracheal intubation was used for this purpose. Mirror laryngoscopy, performed in our hospital on Sept. 22, 1953, revealed granuloma laryngis of the right vocal cord, localization atypical near the posterior end of the cord, and slight hoarseness which patient explained started after the surgery. I ordered physical rest and silence. Patient remained in the hospital for six months on conservative treatment and rest cure. During this time, mirror laryngoscopy was performed several times. Last mirror laryngoscopy was on April 1, 1954; granuloma had disappeared; voice was normal.

CASE 3.—A 28-year-old woman. Mirror laryngoscopy, January, 1954; no pathological findings. Bronchoscopy, February, 1954; mirror laryngoscopy, March 21, 1954; no pathological findings. Tracheal intubation, three and one-half hours' duration, August, 1954. Mirror laryngoscopy in October, 1954; granuloma laryngis, symmetrically on both vocal cords, with atypical localization close to the posterior ends of the vocal cords, each about 3 mm. in diameter; slight hoarseness; respiration normal. Silence and physical rest ordered. On Nov. 24, 1954, the patient reported that during the night she had coughed out some reddish corpuscle. She had thrown it out and mirror laryngoscopy revealed that the granuloma of the left vocal cord had disappeared. After a series of mirror laryngoscopies, the granuloma of the right vocal cord showed symptoms of shrinkage. On Jan. 20, 1955, only a trace of protuberance was noticeable, and, on March 16, it had definitely disappeared. Mirror laryngoscopy; no pathological findings; voice normal.

CASE 4.—A 50-year-old man. Bronchoscopy in February, 1954, (no previous mirror laryngoscopy); mirror laryngoscopy, the end of February, 1954: hyperemia laryngis. Thoracotomy with tracheal intubation of one and one-half hours' duration on March 26. Mirror laryngoscopy, May 21, revealed pedunculated polyp arising from below the middle third of the left vocal cord; maximal diameter about 6 mm. Voice acquired, on phonation, a somewhat vibrating character, and one could see the polyp oscillate to-and-fro on mirror laryngoscopy. Other than this vibrating character of the voice, the floating polyp caused the patient no trouble whatsoever in speech or breathing and he did not agree to have it removed. He left the hospital with the state of the polyp unchanged. The polyp had a reddish appearance; no erosion or exulceration was seen at any of the routine examinations. Physical rest and silence were ordered for the whole period of observation.

CASE 6.—A 39-year-old man. Mirror laryngoscopy, April 16, 1952; no pathological findings. Lobectomy with tracheal intubation of over three hours' duration on June 15. Mirror laryngoscopy, performed in August, revealed a hemispheric sessile reddish growth on the left vocal cord (close to the commissura anterior); diameter about 4 mm.; slight hoarseness. On a regimen of physical rest and silence, the growth and the hoarseness disappeared during the next three months.

CASE 10.—A 24-year-old man. Elsewhere, patient underwent three chest operations for TB of the lungs, each time with tracheal intubation. After admission: bronchoscopy (with no previous mirror laryngoscopy), June 1, 1956; mirror laryngoscopy (in July) revealed a granuloma laryngis of the right vocal cord with typical localization; diameter, 6 mm.; no erosions or exulcerations. Patient underwent another chest operation in our hospital with tracheal intubation of one hour's duration. The clinical symptoms caused by the growth were insignificant, and the patient did not care to have it removed. The growth was reduced to 2 mm. in diameter by the time the patient left the hospital in March, 1957. Silence was kept by the patient during the period of our observation.

CASE 11.—A 40-year-old man. Bronchoscopy, June 1, 1956; chest surgery with tracheal intuba-

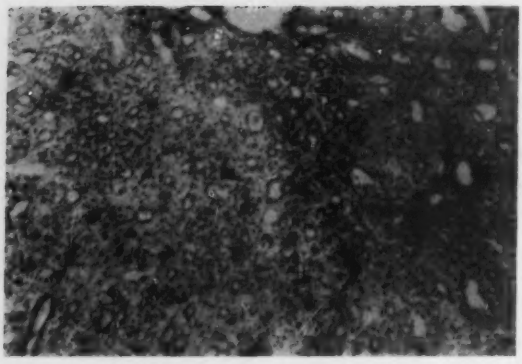

Fig. 1.—Slightly inflammatory, highly vascular granulomatous tissue.

tion of two hours' duration, July 1; mirror laryngoscopy, Sept. 15, revealed a sessile granuloma laryngis of the left vocal cord with typical localization. On a regimen of physical rest and silence, and on a follow-up of seven months, this growth of 3 mm. in diameter shrank almost entirely. Clinical symptoms were negligible.

Case 14.—A 65-year-old woman appeared in my office on March 28, 1956. She gave a history of having undergone surgery for a kidney condition at the University of Hadassah hospital in Jerusalem, in 1955. According to information received from the anesthesist, the tracheal intubation took about two hours. Previous to this surgery, the patient had never suffered from any throat troubles and her voice, speech, and breathing had always been normal. A general check-up revealed no pathological findings, except a scar in a place typical for the operation she had had. Her present complaint was intermittent attacks of severe dyspnea. They had begun several months after the surgery. Mirror laryngoscopy revealed a pedunculated multilobular nonexulcerated growth near the anterior end of the left vocal cord, about 8 mm. maximal diameter. Its appearance was gray. It floated down and up on respiration and phonation. I removed it totally in indirect laryngoscopy. Physical rest and silence were ordered. A check-up after six weeks showed no trace of a growth. The attacks of dyspnea have entirely disappeared. The record of the pathologist (Dr. Reif) stated:

"The microscopic examination shows a highly vascular loose granulomatous tissue. It is strikingly rich in plasma cells. The tissue is partly lined by a regular stratified flat epithelium. No specific inflammatory changes have been found. The picture is obviously one of a chronic process." (Fig. 1 and 2)

The surgical Department of our hospital (Head, Dr. Z. Herman) was helpful in supplying the data concerning surgery and endoscopy.

Comment and Conclusions

As can be seen, the location of the granulomas in my cases were not always "typical." That means, they were not always placed on the medial aspect of the vocal process of the arytenoid cartilage. The "lightly drawn muco-perichondrium of that region" may present a predisposing factor for traumatic reaction, but apparently, it

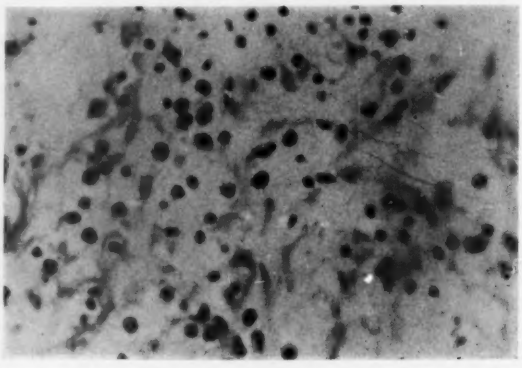

Fig. 2.—(Large magnification): Inflammatory granulomatous tissue rich in plasma cells.

is not always an essential and decisive prerequisite for the production of the granuloma. In some instances, we found the growth in the middle part; in some, at the posterior end or close to the anterior commissure of the vocal cords. In one case (No. 4), the root of the polyp was located on the subglottic surface of the vocal cord.

The granulom does not always evolve a pedunculated polyp and stops at its sessile broadbased stage.

Unpleasant, let alone dangerous, complications described in the literature (e.g., paralysis, hemorrhage, laceration of vocal cords, or even perforation of the trachea), causing the need for a lifesaving postendoscopic bronchoscopy or tracheotomy did not occur in our statistics. Nor did such sequelae like belated tracheal webs develop. It is true, however, that all my cases were adult patients, and most of the above-mentioned complications occurred in infants and children, where they might have been owing, inter alia, to the particular susceptibility of the laryngeal and tracheal mucosa to traumatic reaction at that age—with resultant complications of unpredictable severity.

For all that, I think that the remarkable absence of subjective derangement and of clinically significant symptoms and findings, as seen in our cases—not to mention the relatively rare occurrence of the granulomas—is due not only to the advanced age of the patient and to the technical faultlessness of the endoscopies (which is taken for granted) but also, and in the first place, to another, twofold factor.

I suggest that our persistent maintenance of the principle of a careful pre-endoscopic, rhinologic, and indirect laryngoscopic assessment of a satisfactory state of the upper respiratory tract (including the paranasal sinuses in general and the larynx proper in particular) is a part of this factor. The clinging to this principle is of paramount importance with candidates for a prospectively protracted tracheal intubation for general anesthesia. Whenever catarrhal, allergic, or even slightly inflammatory conditions like hyperemia have been diagnosed, endoscopic procedures, and particularly tracheal intubation, have been postponed (when possible) till return to normal.

The second, but no less important, aspect of this twofold factor is postoperative physical rest and silence on the part of the patient and a systematic laryngoscopic check-up along the lines sketched above, aiming at an early diagnosis of any pathology of the larynx, including a beginning granuloma.

The period of advisability of such a regimen is to be assessed for each case individually. Under this arrangement, the development of a granuloma will often be prevented, and in case it makes its appearance, its self-containing and involutionary trend will be promoted and enhanced. Only exceptionally will removal be necessary, as in Case 14.

Summary

Eight cases of intubation granulomas are reported. It is suggested that, by persistent preoperative rhinolaryngoscopic screening of candidates for tracheal intubation as to catarrhal, allergic, and inflammatory conditions of the upper respiratory tract and the larynx, as well as by scrupulous postoperative similar check-up and by physical rest and silence (observed by the patient in the convalescent period), the number of intubation granulomas can be reduced and their clinical picture considerably eased. Under such conditions, there prevails a natural trend of these growths towards involution, and only exceptionally will their removal be called for.

Renaming of the intubation granuloma "Endogranuloma" is suggested.

5 Rosenbaum St.

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Foreign Body of Retropharyngeal Space

L. REED CRANMER, M.D., Toledo, Ohio

Although pharyngeal and esophageal foreign bodies are not uncommon, the following unusual foreign body is reported because of its unique site of entrance, route of passage, final location, and interesting history.

Report of Case

The patient was a 64-year-old white man who was first seen by his physician in January, 1957, complaining of a feeling of constriction in his throat and soreness which had persisted for the previous month. He was referred to an otolaryngologist, who reported his throat to be normal.

In October, 1957, he was involved in an automobile accident in which his car was struck from behind. He sustained what was diagnosed as the whiplash type of injury. He continued to have persistent cervical pain but no dysphagia or expectoration of blood. Because of the continuing symptoms, x-rays were taken which revealed the presence of a nail apparently in the throat (Figs. 1 and 2). At the time of the accident, there was no history of penetrating injury, nor did he recall holding a nail in his mouth. He denied swallowing a nail, either before or during the accident. Also, he could remember no episodes of choking, severe sore throat, or dysphagia.

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At the time of hospital admission, in November, 1958, the only history of trauma or operations that could be elicited was a herniorrhaphy 20 years previously and an appendectomy 45 years previously. The systemic review revealed frequent epistaxis in the past and arthritis of the hands.

On examination, only a very slight bulge of the posterior pharyngeal wall could be detected about a half of a centimeter to the left of the midline just above the level of the tip of the epiglottis. On palpation this was firm and slightly tender. After study of the x-rays it seemed that this was the probable location of the head of the nail.

On Nov. 15, 1958, the patient was anesthetized and intratracheal intubation used. The patient was placed in the Rose position with the head hyperextended, and the McIvor mouth gag with attached tongue depressor was used for exposure. A 2 cm incision was made in the direction of the constrictor fibers through mucous membrane, submucosa, and constrictor muscle layers. The nail head was found, surrounded by a tough fibrous capsule, lying deeply in the posterior pharyngeal space and extending inferiorly and laterally, imbedded in the prevertebral muscles. Because of the rough rusted surface it was freed and removed with some difficulty (Fig. 3).

Figure 1

Figure 2

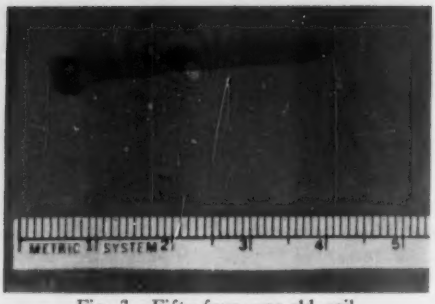

Fig. 3.—Fifty-four-year-old nail.

It seemed inconceivable that the nail could have reached its deep location by ingestion. It was felt that it must have penetrated the tissues as a missile. On recovery from anesthesia this was explained to the patient. He was then able to recall that as a boy of 10 to 12 years of age he and his friends often put such objects as nails, screws, and bolts in the barrel of a 22-gauge rifle. They would even remove the lead bullet from its shell and insert the head of a roofing or lathing nail. On one occasion he had been struck over the root of the nose but thought that it was a glancing blow and failed to tell his parents, probably fearing punishment. Careful reexamination of his face confirmed that there was a scar with underlying depression of the bone at the upper part of the bony nasal bridge. On looking at the lateral skull x-ray one can easily imagine the curving path of the nail on the under surface of the skull.

1838 Parkwood Ave. (2).

Cerebrospinal Otorrhea

EMANUEL M. SKOLNIK, M.D., and JOSE L. FERRER, M.D., Chicago

Escape of cerebrospinal fluid from the ear is indicative of pathologic communication between the subarachnoid space and temporal bone. Leakage is usually a result of temporal bone fractures and occasionally follows surgical trauma or infection. However, in the absence of trauma or infection, and in the light of present knowledge of temporal bone embryology, the rare possibility of congenital dehiscences responsible for "liquor tympanum" must be considered.

The purpose of this presentation is to discuss the conditions responsible for cerebrospinal otorrhea, the mechanism involved, complications which may ensue, and to develop further the concept of congenital pathogenesis.

Fractures of the temporal bone accompanied by dural tears are the commonest causes of cerebrospinal otorrhea.[1] Distinction must be made between instances in which there is an intact tympanic membrane and those in which the membrane is ruptured. The latter, occurring in the presence of an existing otitis media or where an acute infection may develop, is a likely subject for the spread of infection into the subarachnoid space with resultant meningitis.

The commonest type of fracture encountered is the longitudinal, or middle fossa fracture, in which the course of the break is parallel to the long axis of the petrous pyramid. Such a fracture usually passes in front of, or at the level of, the external auditory canal and terminates at the anterior foramen lacerum in the region of the Gasserian ganglion. The middle ear is almost always injured, usually associated with a lacerated tympanic membrane. The incus may become dislocated and, on occasions, a facial paralysis may result.

Interruption of continuity in the ossicular chain results in moderate to severe conductive hearing loss and occasional vertigo. The bony labyrinth in longitudinal fractures is usually spared unless there is a coexistence of a transverse fracture. Fissures are frequently found between the windows, the footplate of the stapes luxated, and the promontory shattered.

Transverse temporal bone fractures are usually found at right angles to and through the pyramid, with consequent damage to the membranous labyrinth. The tympanic membrane is rarely ruptured, but the actual severance of nerves in the internal auditory meatus is not infrequent. Injury to the cochlear and vestibular components is the rule, with resultant complete loss of function.

Important to bear in mind are the microscopic fractures which are not radiographically visible but may have serious implications in the presence of infection, either primary or secondary. Danger of meningitis, early or late, is always to be considered whenever open communication exists between the subarachnoid space and the middle ear, and injuries without obvious intracranial impairment must not be regarded with complacency.

Persistent cerebrospinal leakage from the ear will tend to lower intracranial tension and facilitate the formation of intracranial blood clots. Cessation of the drainage may result in increased intracranial pressure and subsequent coma.[2] The brain, although displaced by hemorrhage or hematoma, may not be compressed so that its function re-

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From the Department of Otolaryngology, University of Illinois College of Medicine.

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mains intact as long as the cerebrospinal fluid escapes.

Pneumocephalus and cerebrospinal fluid fistulas are manifestations of the same underlying pathologic state. The presence of air in the intracranial cavity, as evidenced on roentgenography, is conclusive proof of a dural tear associated with the temporal bone fracture. When undoubted evidence exists, dural repair by the use of fascia lata grafts can be accomplished.[3] This type of repair applies to dural tears associated with fractures of the middle ear and mastoid as well as those of the anterior fossa.

The history of injury with associated cerebrospinal otorrhea and presence or absence of pneumocephalus is incontrovertible evidence of dural rupture. Cerebrospinal fluid from the ear can be identified by analysis of its sugar content (sugar reducing test). However, this analysis is unreliable when, in recent injuries, discharging cerebrospinal fluid is combined with blood or serum. An adjunct to diagnosis, as was carried out in the case being presented, is the instillation of a dye into the spinal canal and observation of its emission from the ear, thereby further substantiating the communication. This technique can also be enlightening in that one may be able to locate the site of the fistula.

The relationship between meningitis and trauma, particularly after an interval of many years, may be established only after searching inquiry. Careful roentgenologic studies may provide significant information, but the exact site of the fracture and dural team may not be known until exploration is undertaken.

Report of Case

A 15-month-old white girl was first observed in December, 1955, having been referred to the Otolaryngologic Clinic of the Illinois Research and Educational Hospitals of the University of Illinois because of "watery" discharge from the right ear.

According to the history, the drainage became evident in July, 1955, unrelated to trauma (either during delivery or later) or infection. The discharge, which was clear, continued unabated. Although no fever was present, the patient had previously been treated by a local physician with antibiotics and the ear packed with cotton. The watery discharge ceased within a few days. However, in September, 1955, the drainage recurred and oxytetracycline (Terramycin) eardrops were employed, and once again cessation of the discharge occurred, only to return one month later.

The child was admitted to a private hospital for observation. X-ray and spinal fluid studies were within normal limits. A pneumoencephalogram and surgery were recommended but refused by the family. The patient was sent home where she developed a fever of 104 F without other signs. Antibiotics were given and within 24 hours the temperature was normal.

Three weeks prior to admission to the R & E Hospitals, the patient became hyperirritable and began losing weight, although to the time of admission the patient had enjoyed good health.

She was admitted because of the "watery" discharge from the right ear. Examination was essentially normal except for the presence of a reddish mass in the external auditory canal, which appeared to be arising from the superior wall of the middle ear. A clinical diagnosis of meningocele was entertained. X-rays of the mastoid revealed a questionable dehiscence of the tegmen tympani on the right. Spinal fluid examination and EEG were normal. The sugar reduction test (Benedict) of the fluid was positive. Culture studies revealed Pseudomonas.

On Jan. 16, 1956, an endaural approach was carried out. The mastoid and middle ear were found to be within normal limits. The ossicles appeared normal, and there was no evidence of a meningocele or dehiscence in the tegmen. Indigo carmine 0.8% was introduced via spinal tap and within a few minutes cerebrospinal fluid (blue) was seen flowing from around the oval window. Temporal fascia was used to cover the dehiscence and a pressure packing applied. The packing was removed 10 days later, and cerebrospinal fluid was observed coming from the previously described site. Skin grafting was performed but to no avail.

A right posterior temporal craniotomy was carried out on June 18, 1956. Exposure of the area revealed a venous-like structure in the area of the upper posterior surface of the petrous bone which appeared to invade the bone. This was coagulated with diathermy and packed with absorbable gelatin sponge. One week later the cerebrospinal otorrhea recurred.

On Aug. 1, 1956, a posterior fossa exploration was again performed and because there was no evidence as to where the defect might be, the internal auditory meatus was packed with absorbable gelatin sponge. Since this procedure was performed, there has been complete cessation of

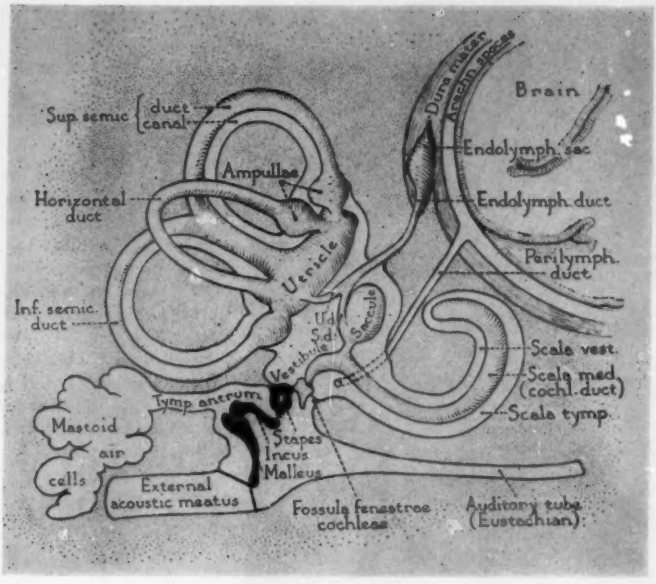

Fig. 1.—General relationships of parts of the internal and middle ear. Reproduced with permission from Bast, T. H., and Anson, B. J.: The Temporal Bone and The Ear, Springfield, Ill. Charles C Thomas, Publisher, 1949.

cerebrospinal otorrhea and the child is well. There is complete absence of vestibular and cochlear function in the right ear.

Comment

Since the history elicited did not reveal trauma or infection that might be held responsible for the cerebrospinal otorrhea, and in the absence of obvious fracture or fistula at the time of the intracranial approach, the possibility of a congenital defect is suggested. It is very possible that there may have been a traumatic incident of which the family is unaware. Also, a dehiscence may have been present, which became obvious following a benign infection.

However, in view of the numerous surgical procedures performed without evidence of a defect and the cessation of the drainage following internal auditory packing, a congenital etiology is to be logically considered.

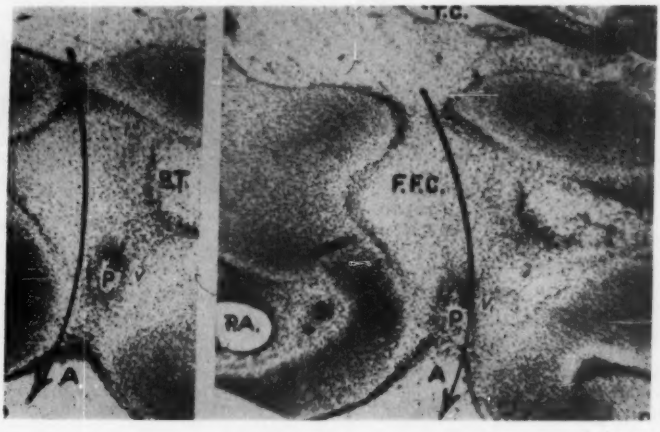

Fig. 2.—Course of the perilymphatic duct and its relationship to the scala tympani and the arachnoid membrane (fetus of 50 mm.). *P.*, Perilymphatic duct. *S.T.*, Scala tympani. *P.A.*, Ampulla of posterior semicircular duct. *T.C.*, Tympanic cavity. *F.F.C.*, Fossula of cochlear fenestra (round window). Reproduced with permission from Bast, T. H., and Anson, B. J.: The Temporal Bone and The Ear, Springfield, Ill., Charles C Thomas, Publisher, 1949.

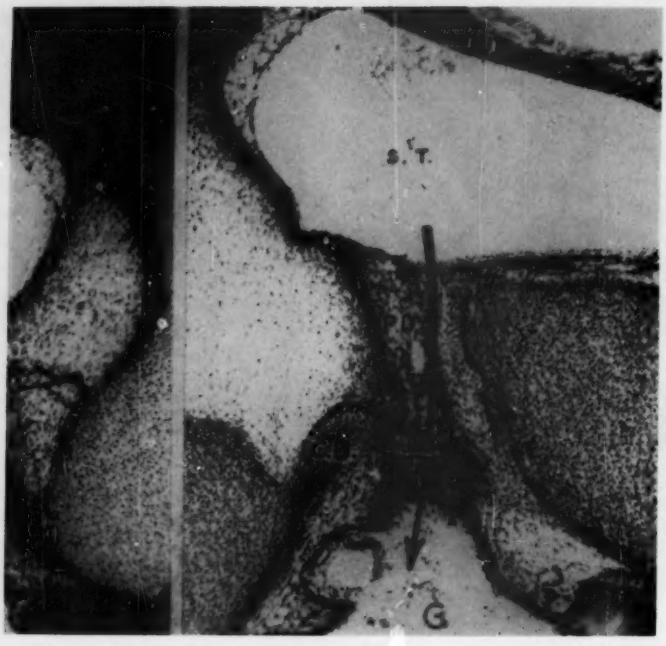

Fig. 3.—Fetus of 84 mm. Presence of a definitive perilymphatic duct. *C.G.*, Cartilage bar. *P.D.*, Perilymphatic duct. *S.T.*, Scala tympani. Reproduced with permission from Bast, T. H., and Anson, B. J.: The Temporal Bone and The Ear, Springfield, Ill., Charles C Thomas, Publisher, 1949.

The anatomic and embryologic relationship to cerebrospinal otorrhea requires elucidation to better understand the pathogenesis of congenital origin. Both the subarachnoid and subdural space extended into the internal ear and indirectly into the brain.

Cochlear aqueduct.—In both children and adults the intermeningeal spaces extend deep into the cochlear aqueduct. Extension of both spaces within the aqueduct varies from case to case (Fig. 1). Frequently the connective tissue of the subarachnoid space extends up to the scala tympani of the vestibular portion of the cochlear where it blends with the periosteum of the scala tympani (Fig. 2). Although, from the anatomic point of view, the cochlear aqueduct furnishes a free communication between the perilymph of the internal ear and the cerebrospinal fluid of the subarachnoid space, in adults the channel is apparently too narrow to encourage a liberal mingling of the two fluids.[4]

Internal Auditory Meatus.—The intermeningeal spaces extend into the internal auditory meatus (Fig. 4). The auditory nerve within the meatus is surrounded by an arachnoid sheath which, at the fundus of the meatus, blends with the dural periosteum of the channel. Where the nerve enters the cavity of the skull, the arachnoid blends with the external layer of the arach-

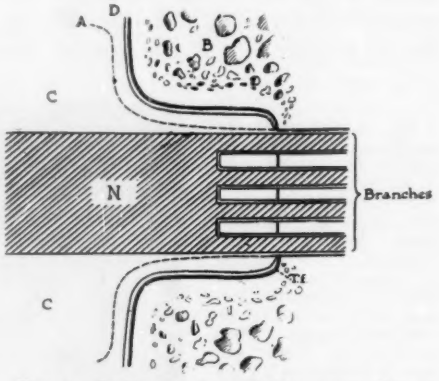

Fig. 4.—Cochlear and vestibular nerves (*N*) in the auditory meatus. *C.*, Cisterna pontis. *A.*, Arachnoid. *D.*, Dura. *B.*, Petrous bone. *T.G.*, Tractus foraminosus. Reproduced with permission from Brunner, H.: Intracranial Complications of Ear, Nose and Throat Infections, Chicago, Year Book Publishers, Inc., 1946.

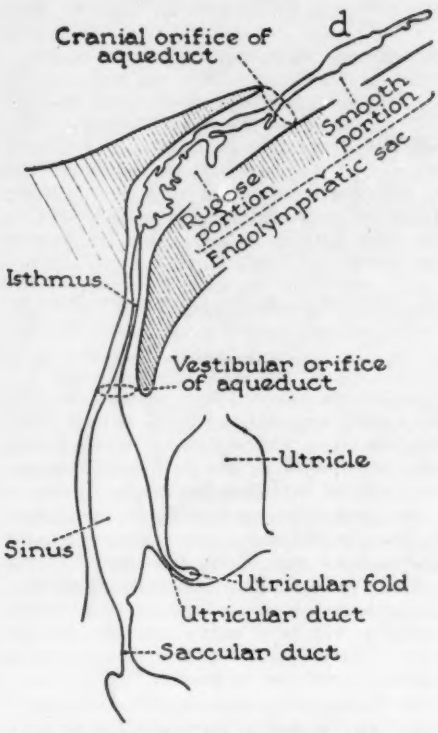

Fig. 5.—Morphological features of the endolymphatic duct system; diagrammatic. Reproduced with permission from Bast, T. H., and Anson, B. J.: The Temporal Bone and The Ear, Springfield, Ill., Charles C Thomas, Publisher, 1949.

noid of the cisterna pontis and the nerve runs through the cisterna pontis toward the medulla oblongata. Another anatomic point of interest is the proximity of cisterna pontis lateralis to the petrous bone, extending from the apex toward the posterior surface of the petrous bone where the internal auditory meatus and cochlear aqueduct drain into the cisterna.[5]

Periotic Space Around Otic Duct.—The otic (endolymphatic) duct (Fig. 5) extends from the point of union of the saccular and utricular ducts, through the otic capsule, to a termination in the otic sac. The otic duct and sac are not surrounded by the periotic labyrinth except proximally, where a short, funnel-shaped diverticulum of the vestibule envelops the otic duct as the latter enters the vestibular aqueduct of the otic capsule. This periotic infundibulum surrounds the otic duct for only a short distance into the intracapsular aqueduct; its derivation represents a spread of the process of vacuolization in the vestibule. The remainder of the connective tissue by which the otic duct and the sac are enveloped possesses no periotic relationship; it assumes the definitely meningeal character of the external (cranial) aperture of the aqueduct.

Summary

Cerebrospinal otorrhea is discussed from both a traumatic and congenital point of view. The pathogenesis of a congenital etiology is elaborated upon, based on anatomical and embryologic fundamentals. Diagnosis and management is considered as well as the complications associated.

1853 W. Polk St. (12).

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Society Transactions

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Jack Allan Weiss, M.D., President
Fletcher Austin, M.D., Secretary

Monthly Meeting, Feb. 2, 1959

Chemosurgical Treatment of Cancer of the Face and Related Structures. Dr. Henry A. Szujewski (by invitation).

Chemosurgery for the treatment of cancer of the face and related structures has been in use for a period of 10 to 15 years and was originated by Dr. Fred Mohs (Mohs, F. E.: Chemosurgery: A Microscopically Controlled Method of Cancer Excision, *Arch. Surgery* 42:279 [Feb.] 1941). The method consists of the application of certain chemicals (zinc chloride + sanguinaria + stibnite) which fix in situ the tissue and prepare it for microscopic examination. Surgery consists of the actual excision by scalpel of tissue for microscopic examination at the time of surgery. This process is continued until all tumor tissue has been removed.

First dichloracetic acid is applied to soften the keratin which usually accompanies tumor growth. A mixture of chemicals (zinc chloride + sanguinaria + stibnite) is then applied and left in place for 24 hours under a cotton-petrolatum dressing. At the end of this time the patient returns and the tumor is excised in layers. As excision is being carried out, frozen sections are made and the tumor identified. If possible, the whole area of tumor is excised initially, or, if it is extensive, it may require several procedures. After treatment is completed, the area begins to slough in a surprisingly short time; in about a week or ten days, the area begins to heal. Usually within two weeks, the area has completely healed with very little scarring.

The method has been used successfully for epidermoid as well as basal cell carcinoma of the nose, eyelid, canthal area, and ala and ear canal. It is also useful in removing tissue which has become cancerous after extensive radiation therapy. Plastic surgery may be necessary after excision of extensive lesions, and the use of a prosthesis may be necessary to completely rehabilitate the patient.

The results of this method of treatment over a ten-year period indicate a five-year survival rate of 100% in those patients who have had no other form of therapy prior to chemosurgery. For the group as a whole, including those who have had other forms of therapy, the percentage is 94.7%.

Discussion

Dr. Arthur Ratko: I have two questions. Can this method be applied to mucosal surfaces? The other question is, why do these lesions look so nice when healed when we can do full-thickness excision and not have them look nearly so nice?

Dr. Irwin Horwitz: This was a very interesting talk. Dr. Schoolman and I, about six years ago, attempted this type of treatment. We used it largely because we had a patient with an inner canthal lesion of one eye who was blind in the other eye. We did a wide exenteration and attempted chemosurgical treatment, but we regret that we did not save the patient.

Dr. Szujewski mentioned that this therapy is easier if the patient has not been treated by other methods. Perhaps our set-up was not elaborate enough. There must be tremendous attention to detail and you must practically have a full-time pathologist in order to use this technique. We found it much easier to do primary grafts than to attempt this method. I do not wish to belittle anything Dr. Szujewski has said, but we can obtain as good results on these ear and eye lesions by our method. However, for some of the lesions about the inner canthus this method may be much better than the application of irradiation or surgery.

Dr. Joseph G. Schoolman: This is a satisfactory method of treatment of carcinoma. It is not the only method but has its place in well-selected lesions.

As Dr. Horwitz indicated, we had trouble with the method. We had a good deal of difficulty with lesions around the corner of the mouth when patients complained of pain because the lesions could not be kept dry. In lesions of the ear, we found a fair degree of associated acute chemical perichondritis. In lesions around the eye, we had a rather large degree of chemosis, but for lesions of the cheek, the method worked very satisfactorily. We have used the method for some cases of postirradiation carcinoma as well as in

cases of radiation necrosis and have had nice results.

This is an excellent method for treatment of selected cases, just as there are selected cases for radiation therapy and for surgical therapy.

DR. HENRY A. SZUJEWSKI (by invitation): The question as to whether we can use this technique on mucosal surfaces is a good one. Yes, we can use it on mucosa if we can get a prosthesis to hold the dressing in place. Let us say the tumor involves the mucosa and is palpable from the outside. We can go in from the outside and excise in total the lesion on the mucosa. I am sure it can also be excised very well by regular surgical excision, but it will not have the benefit of microscopically controlled surgery.

In regard to Dr. Horwitz' and Dr. Schoolman's use of chemosurgery, I wish to say that I do not believe they have had the proper set-up to handle these problems. If you have the proper facilities, there are no problems with this technique. As far as the pathologist is concerned, I have learned to read my own frozen sections. There are pathologists who interpret these frozen sections effectively, especially when they are familiar with your problem. You must have the frozen sections interpreted at the time the excision is being done, and you, the surgeon, must have complete control of the situation.

Dr. Schoolman is right in saying that this method is not effective in treatment of all types of tumors. There are definite limitations to its use. One of the greatest limitations to the use of this method is the fact that the person using it must be well trained and have a great deal of experience. He should also have a broad knowledge of tumor pathology and general surgery. However, I would say that this method, used in conjunction with the microscope, is as useful in the treatment of carcinoma as the stethoscope is in the treatment of heart disease.

Some New Aspects of Vestibular Physiology. PROF. G. DOHLMAN.

The sensorials of the inner ear developed early as superficial orifices and then became better organized to serve different needs for communication. This process, then, definitely is a specialized one from developmental to operational and functional. The sensory epithelium of the hair cell is covered by a gelatinous structure. Some of the basic physiological problems in relation to the function of these sense organs were discussed; namely, how mechanical movement of the fluid within the cochlea may be transformed into sound waves. For some time it has been thought that the bending of the hairs of the hair cells in the sensory epithelium is the basic process in production of sound waves, which, in turn, gives rise to stimulation.

In 1855, Brown raised the question of sensory reactions in the semicircular canal, and it was believed that pooling of the endolymph in the labyrinth produced by rotation of the head was the stimulating agent. Twenty years later, Yevalt made it clear that the reaction took place in the ampulla and that bending of the hairs of the hair cells in one direction or the other through the endolymph caused stimulation. In 1930, Steinhausen, by injecting India ink into the cupulas of living animals, was able to demonstrate flow of the ink into the semicircular canal down into the ampulla. The ink could not flow further without bending the cupula to some extent. Therefore, it was postulated that the cupula and, in turn, the hairs of the hair cells are moved by the movement of the endolymph in the semicircular canal. This would seem to be the only possible physical change at the level of the sensory epithelium. Thus, the mechanism of stimulation is thought to be vibration of the hair cells. Mechanical stimulation of the hair cells in the organ of Corti indicates that stimulation of the sensory epithelium is, in turn, transformed into electrical energy. This concept of the bending of the hairs of the hair cells of the cupula seems to be valid in the light of present knowledge.

Various experimental studies carried out more recently have indicated that the vibration of the organ of Corti and the cupula is not essential to the production of sound, but rather deflection of the hairs of the hair cells in one direction to produce an increased positive electrical potential and deflection of the hair cells in the other direction to produce a negative electrical potential are necessary. In order to study this process, radioactive S-35 has been injected in the semicircular canal to determine the metabolism of the endolabyrinthine fluid. Otoradiographs seem to indicate that the endolymph is secreted in the sensory epithelium and that it contains a high proportion of mucopolysaccharides, which are known to bind the positive ions of potassium. Movement of this fluid, with its electrolytes and positive ions, results in a flow potential. Thus, motion of the endolymph in either direction causes a displacement of the more loosely bound potassium ions in the direction of the motion, producing a concentration of these ions which results in a change in the electrical potentials.

Discussion

DR. SHERMAN L. SHAPIRO: If I understand Dr. Dohlman correctly, Steinhausen's experiment, which he repeated, corroborated the hydrodynamic theory. How does he fit in the new experiments presented here with this theory?

I should also like to know what effect, if any, these studies will have on the vestibular tests now used in clinical practice.

DR. JOHN J. BALLENGER: I am sure we all have enjoyed Professor Dohlman's presentation a great deal. We are greatly indebted to him for helping us to understand these things.

I recall from my student days reading about an experiment on crayfish in which iron filings were placed within the ampulla. A magnet was used to change the position of the iron filings and the resulting changes in head position were traced. Did this cause motion of the fluid, or did it cause movement of the membrane of the cupula?

DR. NICHOLAS TOROK: As Professor Dohlman pointed out, the fundamental work in vestibular physiology was done some 70 or 80 years ago. Since these early times there have been slight and only scattered improvements in our knowledge of the physiology of the vestibular part of the labyrinth. Professor Dohlman's present discovery is a great step forward in this respect.

I wish to ask one question. As long as there is molecular motion within the endolymph, that is, a moving heavy mucopolysaccharide molecule which is basically responsible for changes in the electrical potential, how do these motions affect cochlear physiology?

As I listened to this most interesting presentation, I remembered the great composer Verdi, who surprised the world in his late retirement age by composing his most magnificent and immortal operas. How lucky we are when Professor Dohlman makes such contributions and discoveries in his very early retirement. No doubt, we can expect further "surprises" in vestibular physiology from Professor Dohlman.

I wish to express my appreciation for having the opportunity to discuss this presentation.

DR. WILLIAM IRONSIDE: I wish to ask Dr. Dohlman a question in connection with the electrical charges due to the mucopolysaccharides. I understand from what you said that the positive potential is increased whether the flow is anterior or posterior.

PROFESSOR G. DOHLMAN (by invitation): If we have a pure solution of mucopolysaccharides, we do not have any potential charges, but we get potential charges when we add electrolytes, that is, positive ions. One other thing: This takes place slowly, that is, movement of the positive ions takes place slowly. Therefore, we have electrical negativity or a drop in positivity. They are balanced in a static state when nothing happens, but if you move in one direction, you collect more positive ions over at one end and have comparatively more negativity at the other end.

Dr. Torok asked how we can explain the mechanism in the cochlea by movement of the perilymph or endolymph. There is an experiment in which a microphone and hyalouronic acid were used. If you talk into the microphone with an electrode in the vestibule, you can get an answer as with a telephone. Therefore, charges are present, and the way chemists explain them is by hyaluronic acid.

The next question was about flow potentials. Dr. Ballenger asked about the experiment on crayfish by Cridle. Up to now I have only tried to explain how I see the transformation of movement of the jelly-like structure which surrounds the cupula, the tectorial membrane, and the hair cell. This will move the cupula in one way or the other, which gives a potential charge along the hairs in one direction or the other. That is, if the potential is raised or lowered, there is an opposite effect on one side of the membrane or the other, which might, for example, be positive outside and negative inside the membrane.

This is a hair cell, and when there is increased positivity at one end of the labyrinth, there is increased negativity at the other end. This stimulating process of a bipotential is another thing. We know that the ganglion cell is the metabolic center of the whole neuron. It pours out important things which make it explode as a bipotential. We know from cholinergic stimulation of nerves what happens in the end spaces and that we have a certain frequency of bipotential and always a resting charge. If you move the cupula in one direction, it may increase negativity, and that must cause some change in the double membrane and in the nerve ending. If you move it in the other direction, you get a much higher frequency. You can do the same thing by the application of a polarizing current. Therefore, by bending the cupula or tectorial membrane, by pushing it upward from underneath or downward from above, we have the same charge around the hair cells as when we bend the cupula in one direction. That is what we do when we change these potentials into alternating current.

DR. BALLENGER: Therefore, it is the flow potential. It is the cupula going back and forth.

PROFESSOR DOHLMAN: We have the hairs of the hair cells in the middle of small canals as seen in a cross section of the cupula. By injecting a small amount of dye and pushing on the cupula, it can be seen to move, mostly up and down. Therefore, it is squeezed in one direction and relaxed in the other direction.

Dr. Shapiro asked about caloric reactions and my work with injection of India ink into the fish labyrinth. When I removed the labyrinths from water and raised them up and was able to show that the cupula bent down to the maximum, I thought this was a caloric reaction. When it was turned in the other direction it changed, and it was a caloric reaction. When I considered that my fingers were perhaps 20-25 C, and the labyrinth was perhaps 10 C, there was an enormous dif-

ference in temperature. This difference in temperature has also been measured in the human labyrinth in live patients. When you consider that the difference in temperature in different parts of the canal is perhaps only 0.1 C, it is very small. If we then consider that the cupula reacts very consistently when it is moved by force not more than half a degree, we must change our concept of this motion. It is, of course, correct that we have endolymph in motion, with the rotation reaction and so forth. We have great interest in determining the amount of energy needed for rotation at the threshold and comparing that with the energy needed for hearing and energy needed for sight, which is probably about the same.

In this slide you see the granules after the injection of radioactive S-35. Here are the leaves of the Pachini revolutions, and in the center we have the nerve ending. Here are the granules of irradiated sulfur.

This is the sensory core in the nerve ending. Here are the collagen leaves. Gray and Hubbard have compared the Pachini revolutions in this sense organ. They have been able to show that there may be impressions on both sides. This impression is a little deeper, but when we see Pachini's resolutions we cannot see any compression movement. It must be fluid movement, and, if that is so, we have a sulfur compound with very large molecules and great fluid movement. You must agree that the surface area which corresponds in weight is between three and four square mμ and the sensitivity is the same.

I believe that is about all there is to say about the clinical and chemical approach to these reactions. I have tried to give you the basic experiments and thought, not only on the theory of bending of the hairs of the hair cells, but also on the other changes which may occur.

Thank you very much.

Books

BOOKS RECEIVED

* **Peripheral Facial Palsy: Pathology and Surgery** (in English). By Karsten Kettel, M.D. Price, not given. Pp. 341, with 127 illustrations. Ejnar Munksgaard Forlag, 6 Nörregade, Copenhagen, Denmark; Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill.; The Ryerson Press, Toronto, Canada, 1959.

* **Vocal Rehabilitation: A Manual Prepared for the Use of Graduates in Medicine.** By Friedrich S. Brodnitz, M.D. Price, $2.00. Pp. 119, with 18 illustrations. American Academy of Ophthalmology and Otolaryngology, 15 Second St., S.W., Rochester, Minn., 1959.

* **Chirurgie Der Verengungen Der Oberen Luftwege.** By Prof. Dr. Aurel Réthi. Price, $6.70. Pp. 119, with 166 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart N, Germany, 1959.

* **Radiodiagnostic en Otologie.** By Michel Portmann, and Georges Guillen. Price, 3.700 fr. Pp. 210, with 146 illustrations. Masson & Cie., 120 Boulevard Saint-Germain, Paris 6e.

* **Das Röntgenschichtbild des Ohres. The Tomogram of the Ear** (in German and English). By Prof. Dr. Karl Mündnich. Price, $15.70. Pp. 123, with 205 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart N, Germany, 1959.

BOOK REVIEWS

Functional Roentgen Diagnosis of the Mediastinum Demonstrating Examples of Bronchiogenic Carcinoma (In German). By Dr. R. Kraus. Price, DM 8.40. Pp. 55, with 33 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart N, Germany, 1958.

This short monograph deals with the various methods of roentgen diagnosis of lesions of the mediastinum. Special emphasis is placed on esophagokymography. Experimental studies show a marked neurovegetative correlation and, with proper nerve block or medication, it is possible to demonstrate early metastatic lesion in this area. The origin of these metastatic nodes is usually from the bronchus.

A Binaural Hearing Test to Elicit Cerebral Hearing Loss (In German). By J. Matzker. Price, $4.25. Pp. 117, with 46 illustrations. Georg Thieme Verlag, Herdweg 63, Stuttgart N, Germany, 1958.

This monograph presents a complicated binaural test for loss of hearing due to pathology, either in the brain stem or the cerebral cortex. A special audiometer is used with a grid that can eliminate either the lower or higher frequencies. It is essentially a descrimination test with the use of 41 test words. The interpretation of the results requires a considerable amount of experience, but this test should be investigated by the audiologists, since it may reveal a great deal of valuable information concerning lesions in the cerebrum or brain stem.

* Will be reviewed.

Directory of Otolaryngological Societies *

FOREIGN AND INTERNATIONAL

Canadian Otolaryngological Society
(Société Canadienne d'Otolaryngologie)

President: Dr. G. Arnold Henry, 170 St. George St., Toronto.
Secretary: Dr. Donald M. MacRae, 324 Spring Garden Rd., Halifax, N. S.

Venezuela Otorhinolaryngology Society

President: Dr. Alfredo Celis Pérez.
Secretary: Dr. Jesús Miralles.

International Association of Allergology

President: Dr. Samuel M. Feinberg, 303 E. Chicago Ave., Chicago 11.
Secretary-General: Dr. José Quintero Fossas, Paseo 313, Vedado, Havana, Cuba

International Bronchoesophagological Society

President: Dr. Jo Ono, Tokyo.
Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40.

International College of Surgeons, Section of Ophthalmology and Otolaryngology

President: Dr. John R. Lindsay, 950 E. 58th St., Chicago.
Secretary-Treasurer: Dr. Louis Savitt, 3403 W. Lawrence Ave., Chicago 25.

International Congress of Audiology

General Secretary: Dr. H. C. Huizing, 182 Oostersingel, Groningen, Netherlands.
Place: Leyden, Netherlands.

International Course in Paedo-Audiology

General Secretary: Dr. H. C. Huizing, 182 Oostersingel, Groningen, Netherlands.
Place: Groningen, Netherlands.

Mexican Society of Otolaryngology

President: Dr. Rafael Giorgana
Secretary: Dr. Carlos Valenzuela, Monterrey 47-201, Mexico 7, D. F.

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Paul H. Holinger, Chicago.
Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40.
Meeting: Seventh Congress, Americana Hotel, Miami Beach, Fla., March 20-23, 1960.

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. Paul H. Holinger, Chicago.
Secretary: Dr. Walter E. Heck, Stanford Hospital, San Francisco 15.
Meeting: Miami Beach, Fla., June 13-17, 1960.

American Academy of Ophthalmology and Otolaryngology

President: Dr. John H. Dunnington, 635 W. 165th St., New York.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100-1st Ave. Bldg., Rochester, Minn.

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.

American Board of Otolaryngology

President: Dr. Gordon D. Hoople, 1100 E. Genesee St., Syracuse 10, N. Y.
Secretary-Treasurer: Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Broncho-Esophagological Association

President: Dr. Verling K. Hart, 106 W. 7th St., Charlotte, N. C.
Secretary: Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3.
Meeting: Deauville Hotel, Miami Beach Fla., March 15-16, 1960. Lake Placid Club, Essex County, N.Y., May 20, 1961. Sheraton-Dallas Hotel, Dallas, Texas, May 1-2, 1962. Boca Raton Hotel, Boca Raton, Fla., April 2-3, 1963.

American Laryngological Association

President: Dr. William J. McNally, Montreal.
Secretary: Dr. Lyman G. Richards, Wellesley Hills, Mass.
Meetings: Deauville Hotel, Miami Beach, Fla., March 18-19, 1960. Lake Placid Club, Essex County, N.Y., May 21-22, 1961. Sheraton-Dallas Hotel, Dallas, Texas, May 4-5, 1962. Boca Raton Hotel, Boca Raton, Fla., March 31-April 1, 1963.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Theodore E. Walsh, 640 So. Kingshighway, St. Louis, Mo.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester 7, N.Y.
Meeting: Deauville Hotel, Miami Beach, Fla., March 15-17, 1960. Lake Placid Club, Essex County, N.Y., May 23-25, 1961. Sheraton-Dallas Hotel, Dallas, Texas, May 1-3, 1962. Boca Raton Hotel, Boca Raton, Fla., April 2-4, 1963.

SECTIONS:

Eastern.—Vice President: Dr. F. Johnson Putney, Philadelphia, Pa.
Meeting: Warwick Hotel, Philadelphia, Pa., Jan. 8, 1960.
(Council—Biltmore Hotel, Jan. 9, 1960).
Southern.—Vice President: Dr. Edley H. Jones, Vicksburg, Miss.
Meeting: Roosevelt Hotel, New Orleans, La., Jan. 15-16, 1960.
Middle.—Vice President: Dr. George E. Shambaugh, Jr., Chicago, Ill.
Meeting: Furniture Mart, Chicago, Ill., Jan. 18-19, 1960.
Western.—Vice President: Dr. Rex L. Murphy, Denver, Colo.
Meeting: Brown Palace Hotel, Denver, Colo., Jan. 22-23, 1960.

American Rhinologic Society

President: Dr. Kenneth H. Hinderer, 402 Medical Arts Building, Pittsburgh 13.
Secretary: Dr. Robert M. Hansen, 1735 N. Wheeler Ave., Portland, Ore.

American Otological Society, Inc.

President: Dr. Robert C. Martin, 384 Post St., San Francisco 8.
Vice-President: Dr. Henry L. Williams, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Lawrence R. Boies, University Hospitals, Minneapolis 14
Meeting: Deauville Hotel, Miami Beach, Fla., March 13-14, 1960. Lake Placid Club, Essex, County, N.Y., May 26-27, 1961. Sheraton-Dallas Hotel, Dallas, Texas, April 29-30, 1962. Boca Raton Hotel, Boca Raton, Fla., April 5-6, 1963.

American Otorhinologic Society for Plastic Surgery, Inc.

President: Dr. Raymond S. Rosedale, 610 N. Market Ave., Canton 2, Ohio.
Secretary-Treasurer: Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y.
Meeting: Deauville Hotel, Miami Beach, Fla., March 6-13, 1960.

American Society of Facial Plastic Surgery

President: Dr. Oscar J. Becker, Chicago.
Vice-President: Dr. Sam H. Sanders, Memphis.
Secretary: Dr. Samuel M. Bloom, 123 E. 83d St., New York 28.
Treasurer: Dr. Joseph C. Miceli, Brooklyn.

American Society of Ophthalmologic and Otolaryngologic Allergy

President: Dr. Michael H. Barone, 468 Delaware Ave., Buffalo 2, N.Y.
Secretary-Treasurer: Dr. Daniel S. DeStio, 121 S. Highland Ave., Pittsburgh 6.

Otosclerosis Study Group

President: Dr. E. P. Fowler Jr., 180 Fort Washington Ave., New York 32.
Secretary-Treasurer: Dr. Arthur L. Juers, 1018 Brown Building, Louisville 2.

Society of Military Otolaryngologists

President: Lt. Col. Stanley H. Bear (MC), USAF, Maxwell AFB, Ala.
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1. Jones, E. H.: Eye, Ear, Nose and Throat Monthly *38*:460, 1959.

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*Hirsch, H. A., and Finland, M.: *New England J. Med.* 260:1099 (May 28) 1959.

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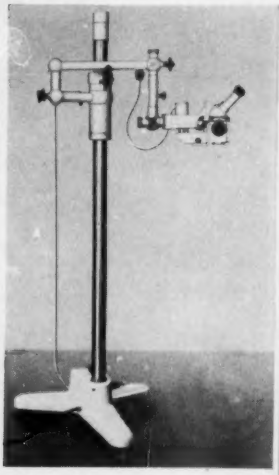

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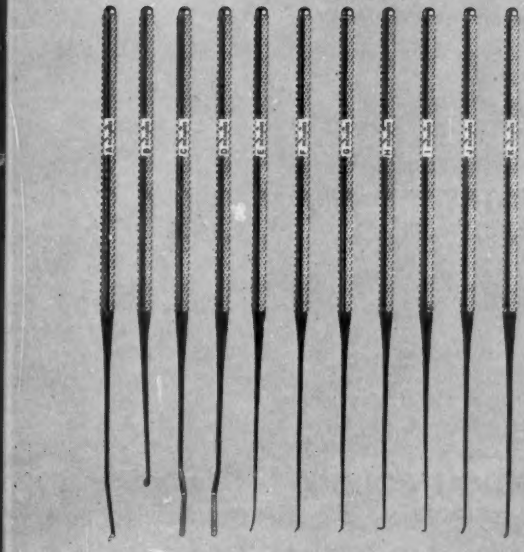

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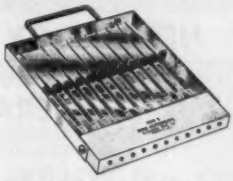

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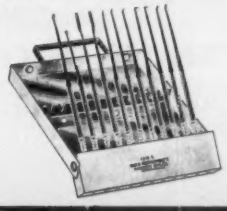

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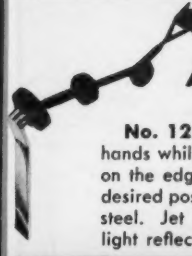

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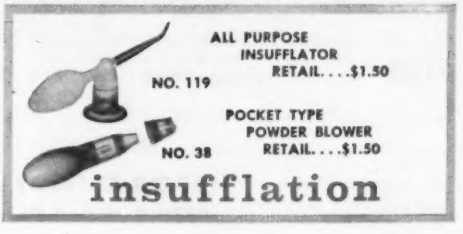

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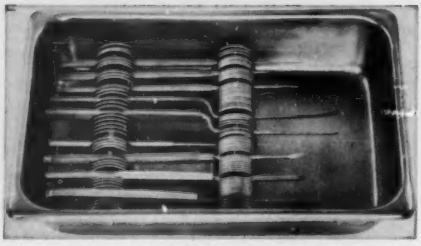

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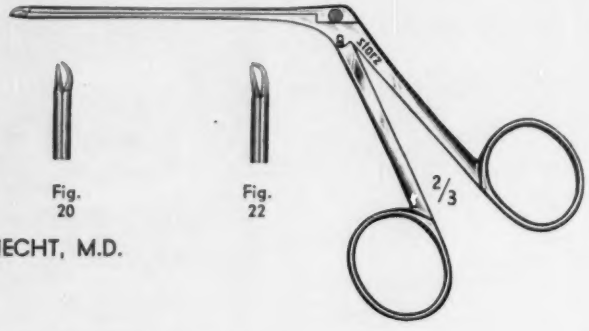

Fig. 20

Fig. 22

N-1698* Fig. 20. Forceps, Wire Tightening, SCHUKNECHT: for tightening wire prothesis about the incus in stapes procedure, straight lower blade, stainless steel **$29.00**

N-1698* Fig. 21. Forceps, Wire Tightening, SCHUKNECHT: lightly angled lower blade, ... **$29.00**

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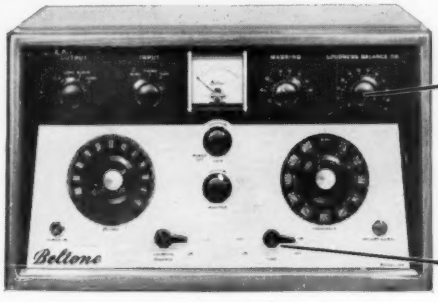

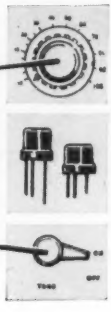

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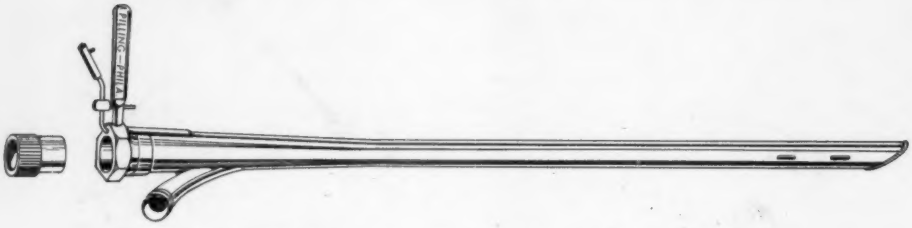

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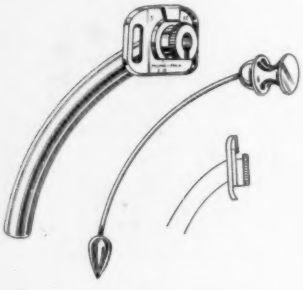

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